

Inventor: Sirbasku

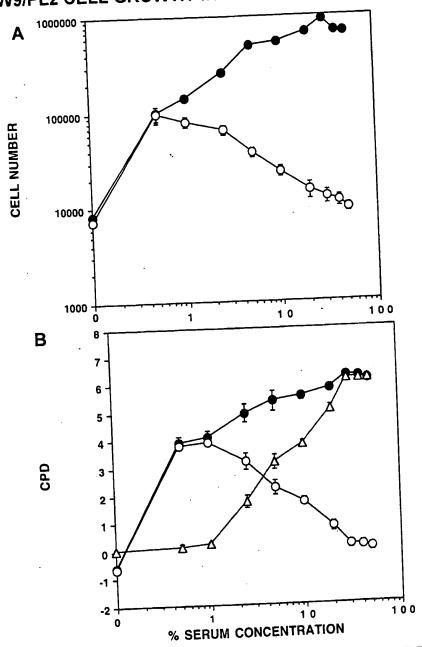
Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 1 of 133

FIGURE 1

MTW9/PL2 CELL GROWTH IN 50% CDE - HORSE SERUM



- A: DATA EXPRESSED AS CELL NUMBER AFTER 7 DAYS Growth with 1.0 x 10^{-8} M E_2 (closed circles) and without hormone (open circles) in medium containing the designated concentrations of serum.
- B. DATA IN (A) EXPRESSED AS CPD

 The symbols indicate the same conditions as (A)
 except the open triangles show CPD differences
 between growth in dishes with and without the
 hormone (Difference = estrogenic effect on growth).

Inventor: Sirbasku

Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 2 of 133

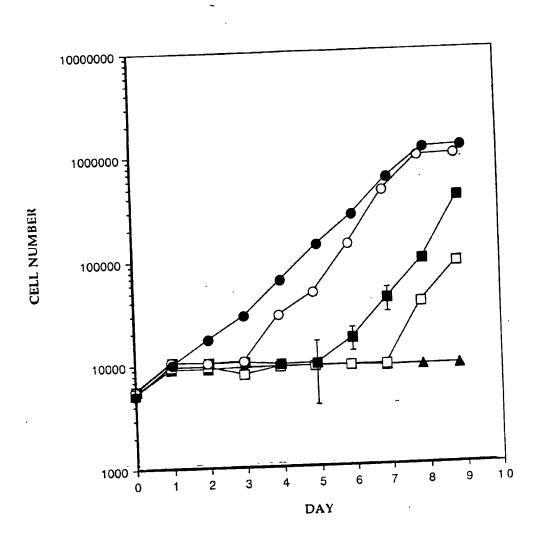
)

H

North adds that that adds

FIGURE 2

MTW9/PL2 CELL GROWTH IN 50% CDE - HORSE SERUM WITH ESTROGENS ADDED AT VARIOUS TIMES AFTER SEEDING



LEGEND:

Control growth in the absence of exogenous estrogen is shown by (triangles). In other dishes, 1.0 x 10^{-8} M E₂ was added at the beginning of the experiment (closed circles), after 48 h (open circles), after 96 h (closed squares), or after 144 h (open squares).

[]

Express Mail EL818623436US

Inventor: Sirbasku

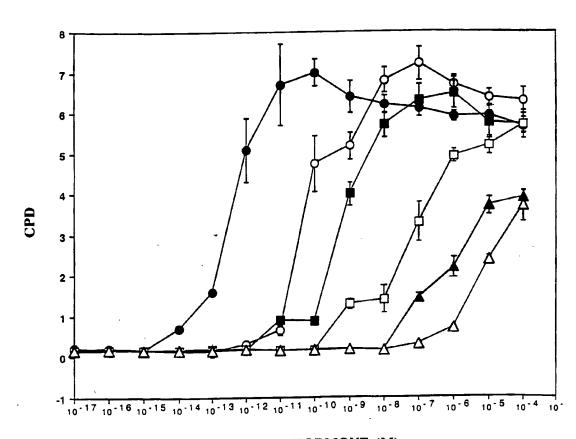
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 3 of 133

FIGURE 3

STEROID HORMONE DOSE RESPONSE EFFECTS WITH MTW9/PL2 CELLS IN 50% CDE - HORSE SERUM



STEROID HORMONE (M)

LEGEND:

Closed circles = E₂
Open circles = E₁
Closed squares = E₃
Open squares = Progesterone
Closed triangles = DHT
Open triangles = T

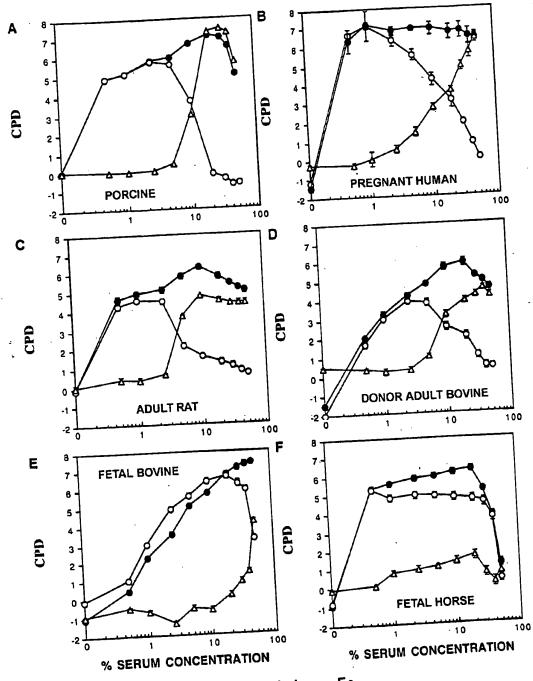
Inventor: Sirbasku

Atty Dkt. No. 1944-0080**0** Contact: C.G. Mintz (713) 238-8000

Page 4 of 133

FIGURE 4

MTW9PL2 CELL GROWTH IN CDE SERUM FROM DIFFERENT SPECIES



LEGEND: Open circles = -E₂
Closed circles = +E₂
Open triangles = Estrogenic effect

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

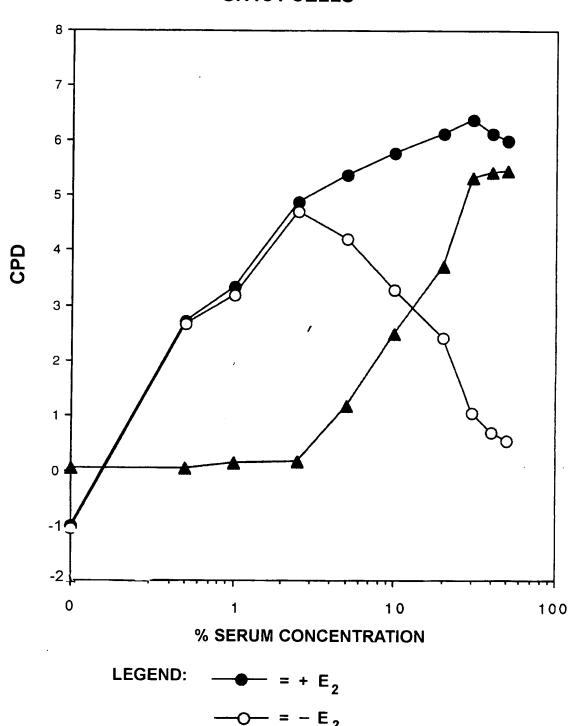
Page 5 of 133

dead stead their time steel from their or the first that their time steel from their or that are final near their could be

M had nad mits that had a start a

FIGURE 5

CDE HORSE SERUM TITRATION GH4C1 CELLS



= Estrogenic effect

3 -i

Express Mail EL818623436US

Inventor: Sirbasku

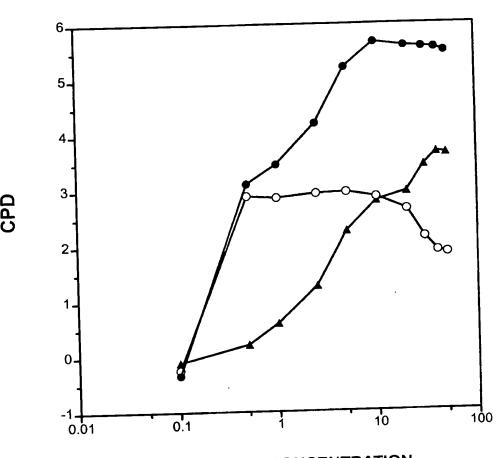
Atty Dkt. No. 1944-0080 **0**

Contact: C.G. Mintz (713) 238-8000

Page 6 of 133

FIGURE 6

ZR-75-1 CELLS IN CDE - HORSE SERUM \pm 10 nM $\,$ E $_2$



% SERUM CONCENTRATION

LEGEND:

Closed circles = +E₂
Open circles = -E₂
Closed triangles = Estrogenic effect

Inventor: Sirbasku

Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

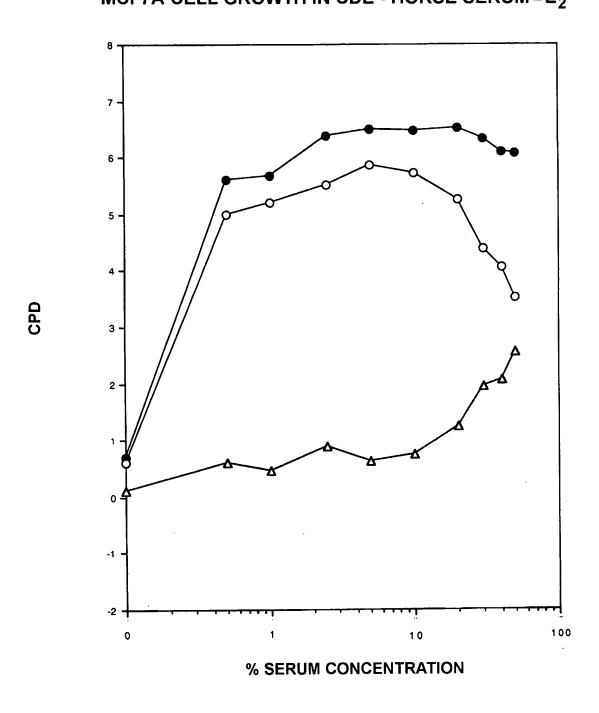
Page 7 of 133

that that that the that the

Horn until 8 H

that the Hall that

FIGURE 7 $\label{eq:mcf7a} \mbox{MCF7A CELL GROWTH IN CDE - HORSE SERUM} \mbox{$^\pm$E}_2$



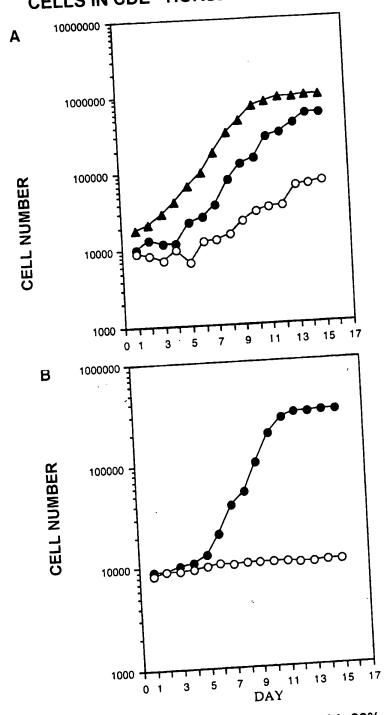
LEGEND:

Closed circles = +E₂ Open circles = -E₂ Closed triangles = Estrogenic effect Atty Dkt. No. 1944-00800 Contact: C.G. Mintz (713) 238-8000

Page 8 of 133

FIGURE 8

GROWTH KINETICS OF T47D HUMAN BREAST CANCER CELLS IN CDE - HORSE SERUM ±10 nM E2



- (A) The growth of the cells in medium with 20% (v/v) serum with 10 nM E₂ (closed circles) and without the steroid (open circles). As comparison, growth is shown in medium containing 10% (v/v) FBS (triangles).
- (B) T47D cell growth kinetics in medium with 50% (v/v) serum with E₂ (closed circles) and without the steroid (open circles).

Inventor: Sirbasku

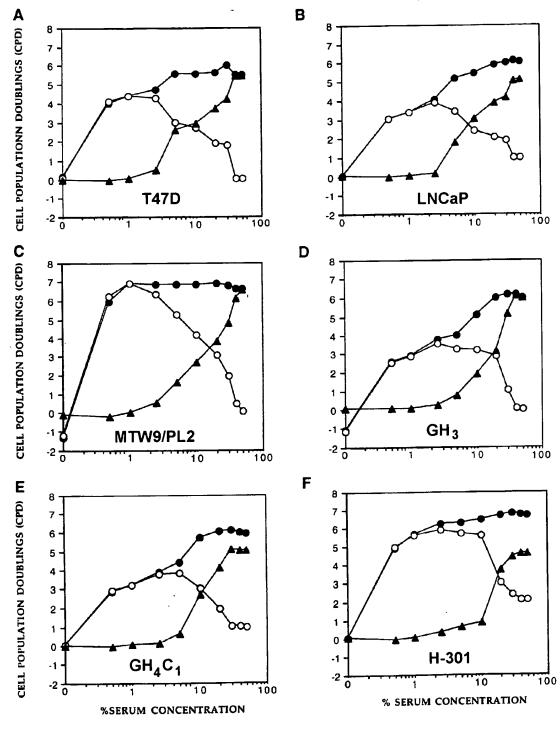
Atty Dkt. No. 1944-0080 **1**

Contact: C.G. Mintz (713) 238-8000

Page 9 of 133

FIGURE 9

GROWTH OF HUMAN & RODENT CELL LINES IN 50% CDE - HORSE SERUM $\pm E_2$ (10 nM)



LEGEND: Closed circles = Medium with 10 nM E₂
Open circles = Medium without E₂
Triangles = Estrogenic effect

Inventor: Sirbasku Atty Dkt. No. 1944-00800

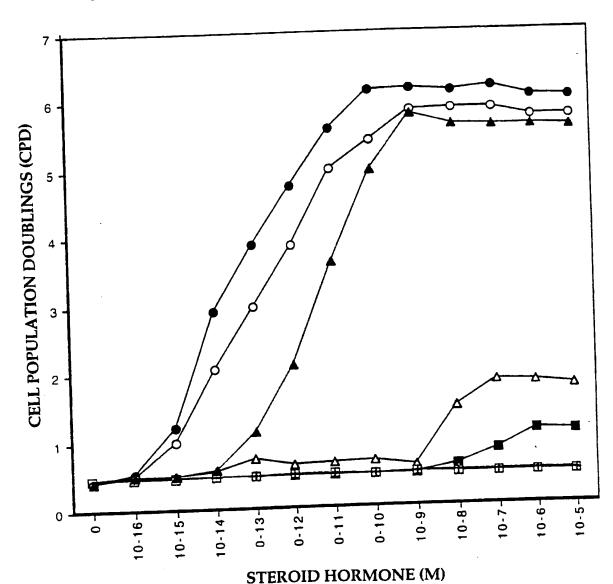
Contact: C.G. Mintz (713) 238-8000

Express Mail EL818623436US

Page 10 of 133

FIGURE 10

DOSE RESPONSE OF STEROID HORMONES WITH T47D CELLS IN 50% CDE - HORSE SERUM



LEGEND:

Growth after 14 days is shown in response to:

Closed circles = E₂ Open circles = E₁ Closed triangl $s = E_3$ Open triangles = DHT

Closed squares = Testosterone Open squares = Progesteron

Hapress Mail EL8-862340008

Inventor: Sirbasku

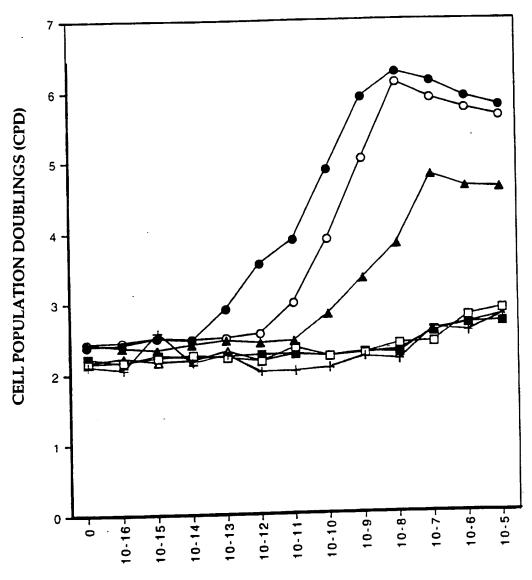
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8

Page 11 of 133

FIGURE 11

DOSE RESPONSE OF STEROID HORMONES WITH H-301 CELLS IN 50% CDE - HORSE SERUM



STEROID HORMONE (M)

LEGEND:

Growth after 9 days is shown in response to:

Closed circles = E_2

Open circles = E₁

Closed triangles = E₃

Open triangles = DHT

Closed squares = Testosterone

Open squares = Progesterone

general construction grows many grown II II sweet party grows and from the first that the first

į.

Express Mail EL818023436US

Inventor: Sirbasku

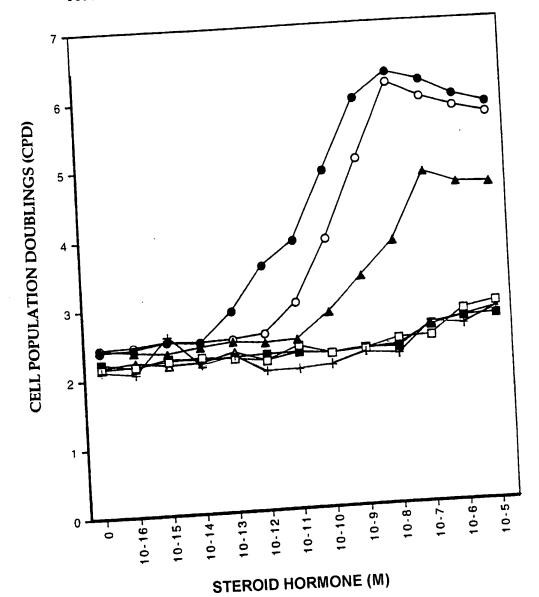
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 12 of 133

FIGURE 12

DOSE RESPONSE OF STEROID HORMONES WITH H-301 CELLS IN 50% CDE - HORSE SERUM



LEGEND:

Growth after 9 days is shown in response to:

Closed circles = E₂

Open circles = E1

Closed triangles = E_3

Op n triangles = DHT

Closed squares = Testosterone Open squares = Progesterone

Inventor: Sirbasku

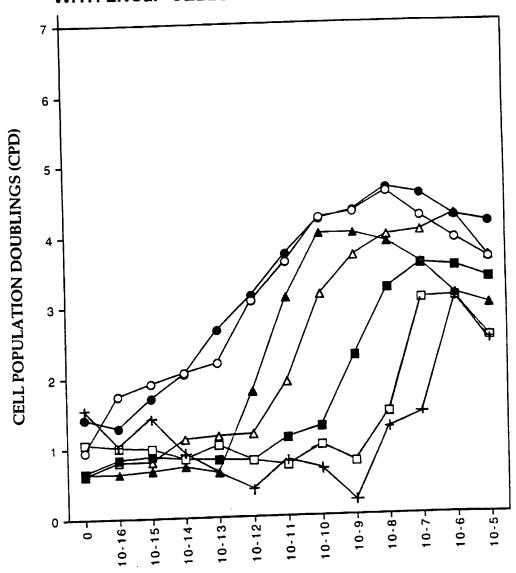
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 13 of 133

FIGURE 13

DOSE RESPONSE OF STEROID HORMONES WITH LNCaP CELLS IN 50% CDE - HORSE SERUM



STEROID HORMONE (M)

LEGEND:

Growth after 14 days is shown in response to:

-

Closed circles = E₂

Open triangles = E_1

Open squares = E_3

Open circles = DHT

Closed triangles = Testosterone

Closed squares = Progesterone

Inventor: Sirbasku

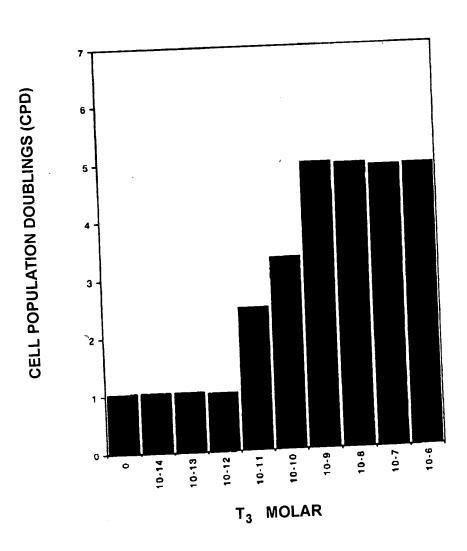
Atty Dkt. No. 1944-0080 **Q**

Contact: C.G. Mintz (713) 238-8000

Page 14 of 133

FIGURE 14

${ m T_3}$ TITRATION OF ${ m GH_3}$ CELLS GROWN IN SERUM - FREE MEDIUM (PCM)



that the many them tends of the third tends of the tends

1-5

Express Mail EL818623436US

Inventor: Sirbasku

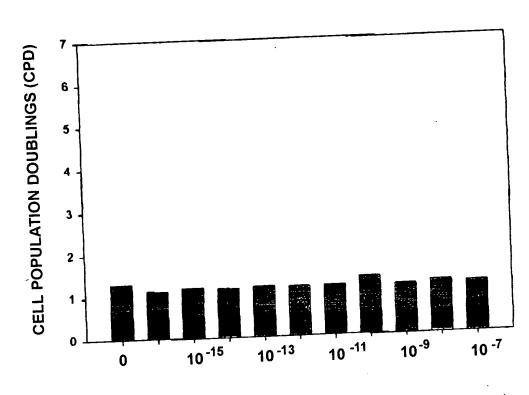
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 15 of 133

FIGURE 15

E_2 TITRATION OF GH_3 CELLS GROWN IN SERUM-FREE MEDIUM MINUS T_3



E2 MOLAR CONCENTRATIONS

Inventor: Sirbasku

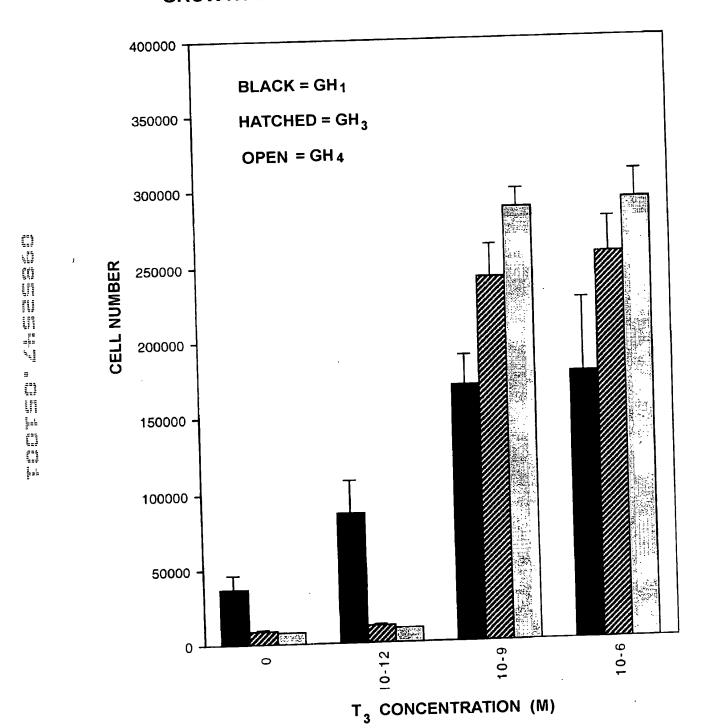
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 16 of 133

FIGURE 16

EFFECT OF T_3 ON GH CELL LINES: GROWTH IN 2.5% CDE - HORSE SERUM WITH NO E_2



Inventor: Sirbasku

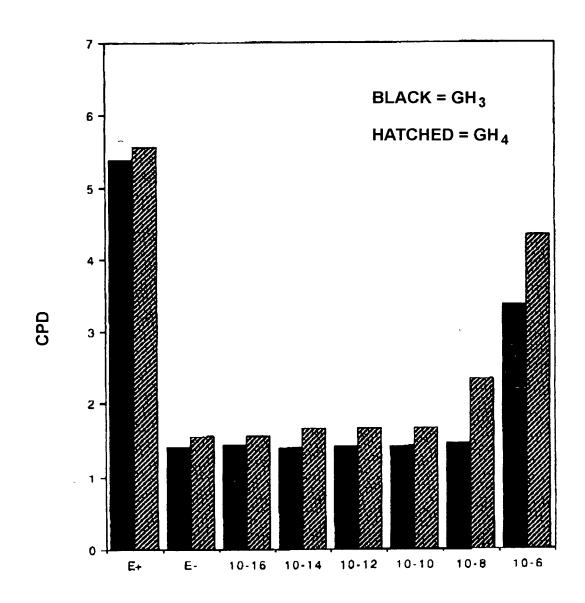
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 17 of 133

FIGURE 17

EFFECT OF T_3 ON PITUITARY CELL LINES INCUBATED IN 50% CDE - HORSE SERUM



T₃ CONCENTRATION

Ē=i

£.}

Express Mail EL818623436US

Inventor: Sirbasku

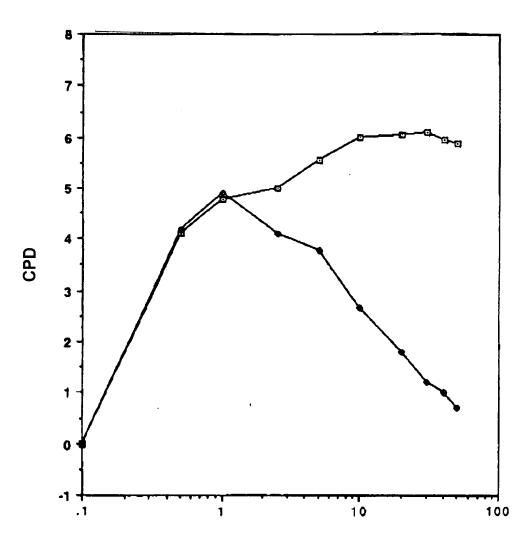
Atty Dkt. No. 1944-0080 **9**

Contact: C.G. Mintz (713) 238-8000

Page 18 of 133

FIGURE 18

EFFECT OF XAD-4 RESIN TREATED HORSE SERUM ON MTW9/PL2 CELL GROWTH ± E₂



% SERUM CONCENTRATION

LEGEND:

Open squar $s = + E_2$

Closed squares = - E₂

Inventor: Sirbasku

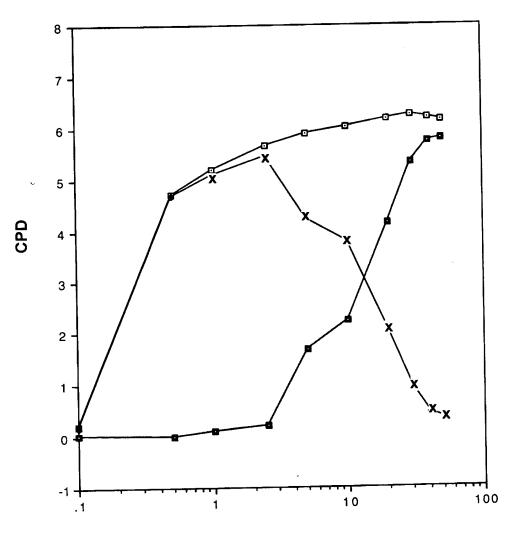
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 19 of 133

FIGURE 19

EFFECT OF XAD-4 RESIN TREATED HORSE SERUM ON T47D CELL GROWTH $^\pm$ E $_2$



% SERUM CONCENTRATION

LEGEND:

Open squares = + E₂

 $XXX = -E_2$

Closed squares = Estrogenic effect

And the first that the first that the same of the same

Inventor: Sirbasku

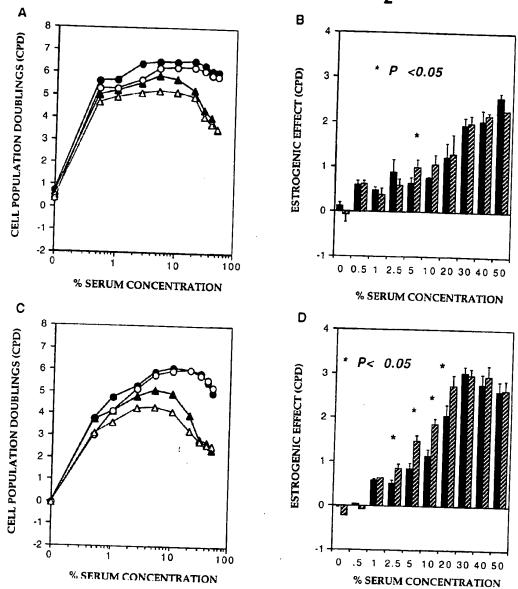
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 20 of 133

FIGURE 20

MCF-7 CELL GROWTH IN CDE - HORSE SERUM ± PHENOL RED AND ± E₂



LEGEND:

(A) MCF-7A cell growth in phenol red containing medium with E_2 (closed circles) and without E_2 (closed triangles), and in phenol red-free medium with E_2 (open circles) and without E_2 (open triangles).

(B) Estrogenic effects with MCF-7A cells in medium with phenol red (solid bars) and without phenol red (shaded bars) were calculated from (A) and defined as the CPD in medium containing E_2 minus the CPD in medium without added E_2 .

(C) MCF-7K cell growth in phenol red medium with E_2 (closed circles) and without E_2 (closed triangles), and in phenol red-free medium with E_2 (open circles) and without E_2 (open triangles).

(D) Estrogenic effects with MCF-7K cells in medium with phenol red (solid bars) and without phenol red (shaded bars), calculated from (C).

ļub

1.1

Express Mail EL818623436US

Inventor: Sirbasku

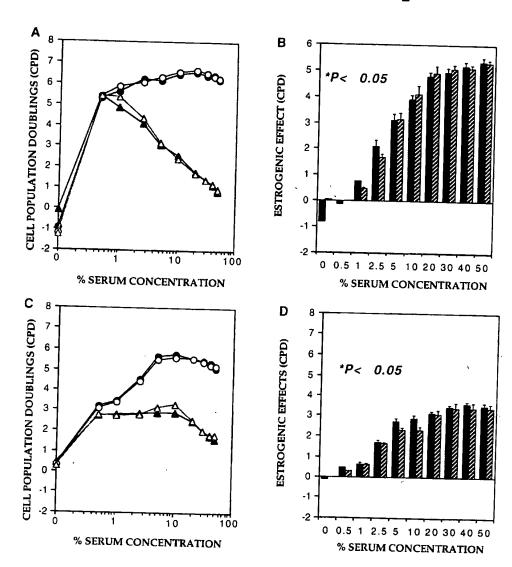
Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 21 of 133

FIGURE 21

T47D AND ZR-75-1 CELL GROWTH IN CDE-HS ± PHENOL RED AND ± E₂



LEGEND:

(A) T47D cell growth in phenol red containing medium with E_2 (closed circles) and without E_2 (closed triangles), and in phenol red-free medium with E_2 (open circles) and without E_2 (open triangles).

(B) Estrogenic effects with T47D cells in medium with phenol red (solid bars) and without phenol red (shaded bars) were calculated from (A) and defined as the CPD in medium containing E_2 minus the CPD in medium without added E_2 .

(C) ZR-75-1 cell growth in phenol red medium with E_2 (closed circles) and without E_2 (closed triangles), and in phenol red-tree medium with E_2 (open circles) and without E_2 (open triangles).

(D) Estrogenic effects with ZR-75-1 cells in medium with phenol red (solid bars) and without phenol red (shaded bars), calculated from (C).

A graph given profess of the state of the st

[]

Express Mail EL818623436US

Inventor: Sirbasku

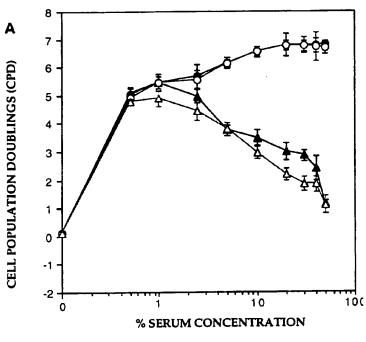
Atty Dkt. No. 1944-0080

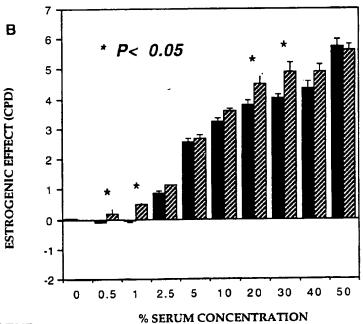
Contact: C.G. Mintz (713) 238-8000

Page 22 of 133

FIGURE 22

MTW9/PL2 CELL GROWTH IN CDE - HORSE SERUM ± PHENOL RED AND ±E₂





LEGEND:

- (A) MTW9/PL2 growth in phenol red medium with E $_2$ (closed circles) and without E $_2$ (closed triangles), and in phenol red-free medium with E $_2$ (open circles) and without E $_2$ (open triangles).
- (B) Estrogenic effects with MTW9/PL2 cells in medium with phenol red (solid bars) and without (shaded bars) were calculated from (A).

Inventor: Sirbasku

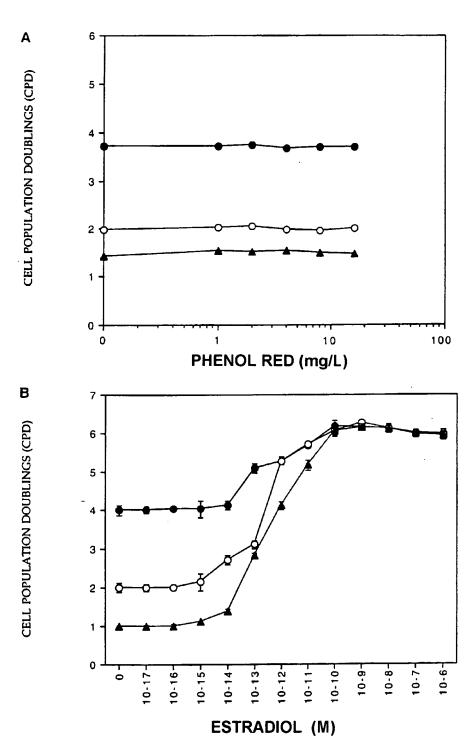
Atty Dkt. No. 1944-0080 🕽

Contact: C.G. Mintz (713) 238-8006

Page 23 of 133

FIGURE 23

DOSE RESPONSE TO PHENOL RED AND E₂ IN THREE CELL LINES



LEGEND: The growth of the MCF-7A (closed circles), MTW9/PL2 (open circles) and T47D (closed triangles) cell lines was assessed at 14, 7, and 12 days.

And the first from th

H

}.b

Express Mail EL818623436US

Inventor: Sirbasku

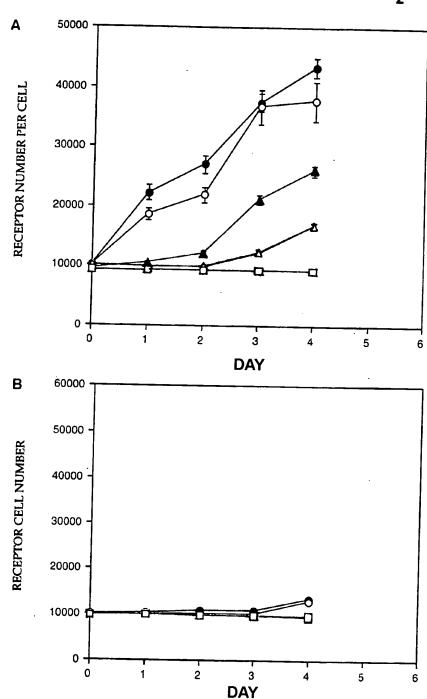
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 24 of 133

FIGURE 24

PROGESTERONE RECEPTOR INDUCTION IN T47D CELLS BY PHENOL RED AND E₂



LEGEND:

(A) The effects of E_2 at 1.0 x 10⁻⁸ M (closed circles), 1.0 x 10⁻¹⁰ M (open circles), 1.0 x 10⁻¹²M (closed triangles), 1.0 x 10⁻¹⁴ M (open triangles) and the control without added E_2 (open squares).

(B) The effects of phenol red at 16 mg/L (closed circles), 8mg/L (open circles), 4 mg/L (closed triangles), 2 mg/L (open triangles), and the control without phenol red (open squares).

Inventor: Sirbasku

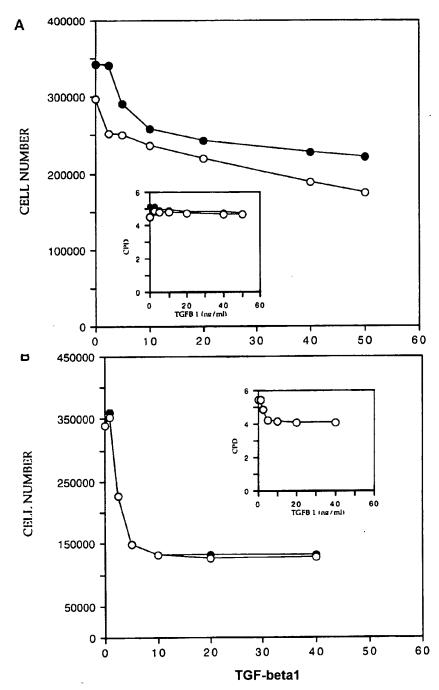
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 25 of 133

FIGURE 25

EFFECT OF TGF-beta1 ON THE GROWTH OF BREAST/MAMMARY ORIGIN CELL LINES



LEGEND:

that the first

Į,

- (A) The effect of the transforming growth inhibitor on human breast MCF-7K cell growth as measured after 12 d either with 10 nM E_2 (closed circles) or without the hormone (open circles). The insert shows conversion of the cell number results to CPD.
- (B) The same experiment with rat mammary MTW9/PL2 cells after 9 d growth.

den been been early them to be to be the second of the sec

C]

Express Mail EL818623436US

Inventor: Sirbasku

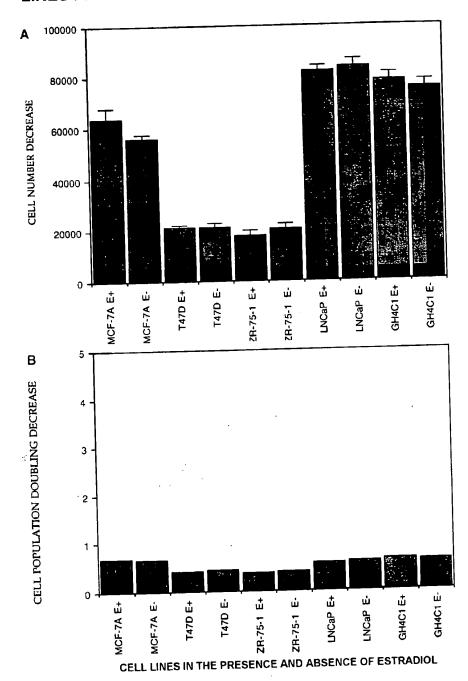
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 26 of 133

FIGURE 26

EFFECT OF TGF-beta1 ON THE GROWTH OF CELL LINES FROM BOTH HUMAN AND RODENT TUMORS



In these studies, TGF-beta1 was added at 40 ng/ml. Estradiol (\pm E) indicates either no added E $_2$ or the steroid at 10 nM.

(A) The effect of TGF-beta1 on five cell lines after 10-14 d growth in medium ± E₂. The results are expressed as cell number decreases caused by TGF-beta1.

(B) The CPD d creases caused by TGF-beta1 $\pm E_2$ with each of the cell lines shown in (A).

Inventor: Sirbasku

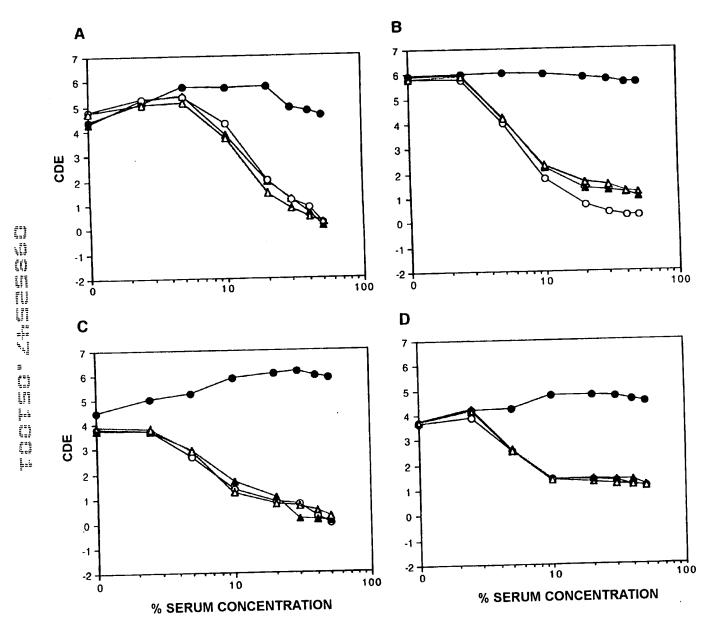
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 27 of 133



EFFECT OF EGF AND TGF-alpha ON THE GROWTH OF HUMAN BREAST CANCER CELLS



The cells were grown in D-MEM/F-12 supplemented with increasing concentrations of CDE horse serum. Each line tested was grown in serum alone (open circles) and in serum plus 50 ng/ml EGF (open triangles), 50 ng/ml TGF-alpha (closed triangles), or 10 nM E_2 without exogenous growth factors (closed circles). (A) - (D) show the results with the MCF-7A, MCF-7K, T47D, and ZR-75-1 cell lines, respectively.

Inventor: Sirbasku

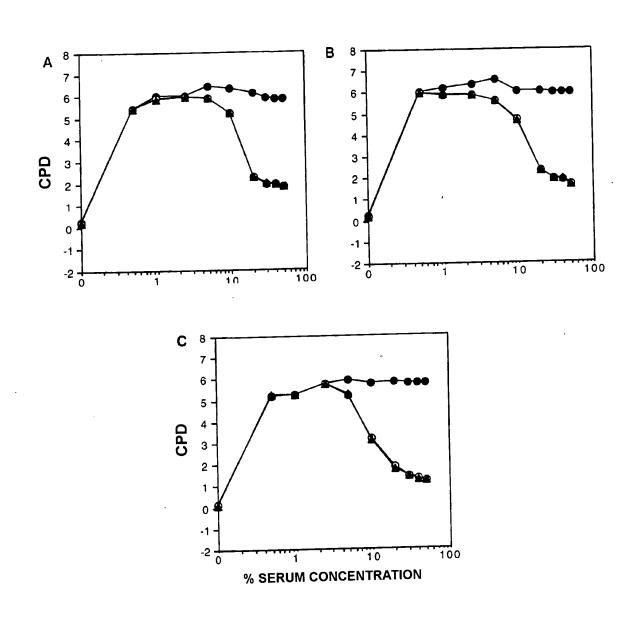
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 28 of 133

FIGURE 28

EFFECT OF IGF-I ON THE GROWTH OF HUMAN BREAST CANCER CELLS



Breast cancer cells were grown in D-MEM/F-12 supplemented with increasing concentrations of CDE horse serum. Each cell line tested was grown in serum alone (open circles) and in serum plus 1.0 ug/ml IGF-I (triangles), or in serum with 10 nM E_2 without exogenous growth factors (closed circles). (A) - (C) show the results with the MCF-7K, MCF-7A and T47D cells, respectively. Assays were conducted for 12-14 d.

T47D

prod alled pinds para south front is it well in the bank bank made there is all at the bank and there is it is well in at

 Express Mail EL818623436US

Inventor: Sirbasku

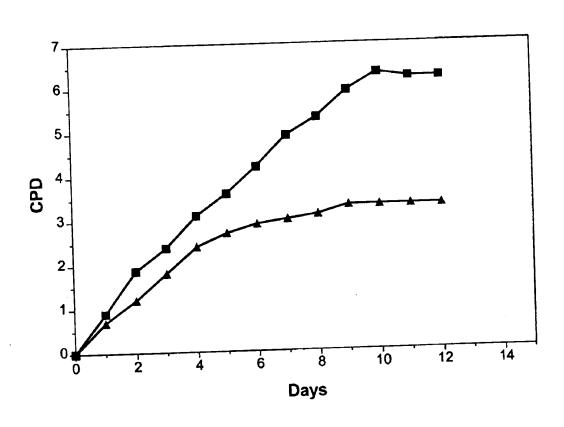
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 29 of 133

FIGURE 29

T47D CELLS IN STANDARD D-MEM/F-12 MEDIUM VS "LOW FE" SERUM-FREE SERUM



LEGEND:

--- "STANDARD" MEDIUM

LOW-FE" MEDIUM

Inventor: Sirbasku

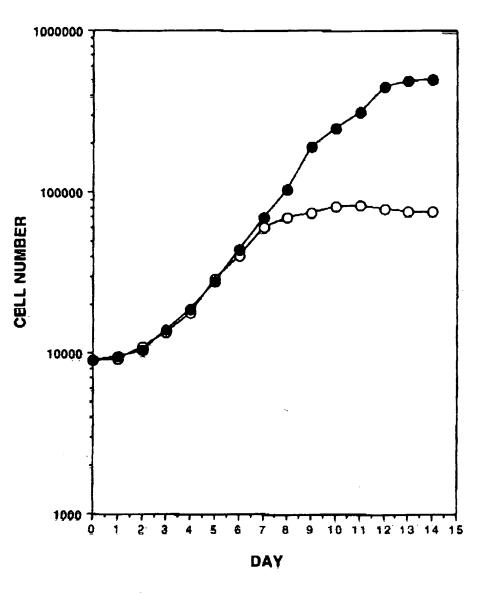
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 30 of 133

FIGURE 30

LNCaP CELLS IN STANDARD D-MEM/F-12 MEDIUM VS "LOW-FE" SERUM-FREE MEDIUM



LEGEND:

"STANDARD" MEDIUM
"LOW-FE" MEDIUM

Į.i.

£.1

Express Mail EL818623436US

Inventor: Sirbasku

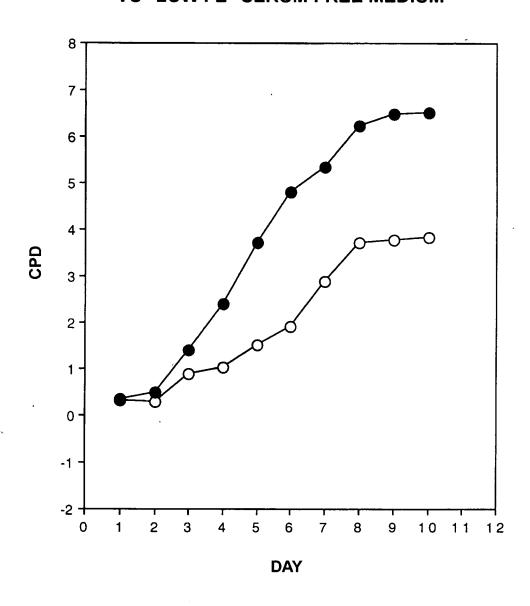
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 31 of 133

FIGURE 31

MDCK CELLS IN STANDARD D-MEM/F-12 MEDIUM VS "LOW FE" SERUM-FREE MEDIUM



LEGEND:

—O- "STANDARD" MEDIUM

"LOW-FE" MEDIUM

The first of the first first of the first of the first ment of the first first

Express Mail EL818623436US

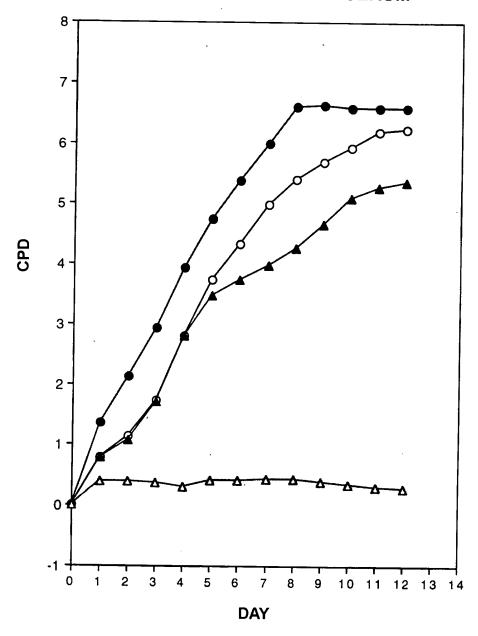
Inventor: Sirbasku Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 32 of 133

FIGURE 32

LNCaP CELL GROWTH IN CAPM ± DHT AND 10% FETAL BOVINE SERUM



LEGEND:

Closed circles = Fetal bovine serum Open circles = CAPM + DHT Closed triangles = CAPM - DHT Open triangles = D-MEM/F12 only

Inventor: Sirbasku

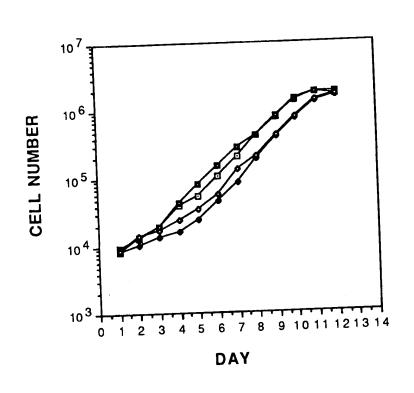
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 33 of 133

FIGURE 33

PC3 AND DU145 GROWTH IN SERUM - FREE MEDIUM VS MEDIUM WITH 10% FETAL CALF SERUM



LEGEND:

PC3 IN SERUM-FREE MEDIUM

DU145 IN SERUM-FREE MEDIUM

PC3 IN 10% FETAL CALF SERUM

DU145 IN 10% FETAL CALF SERUM

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 34 of 133

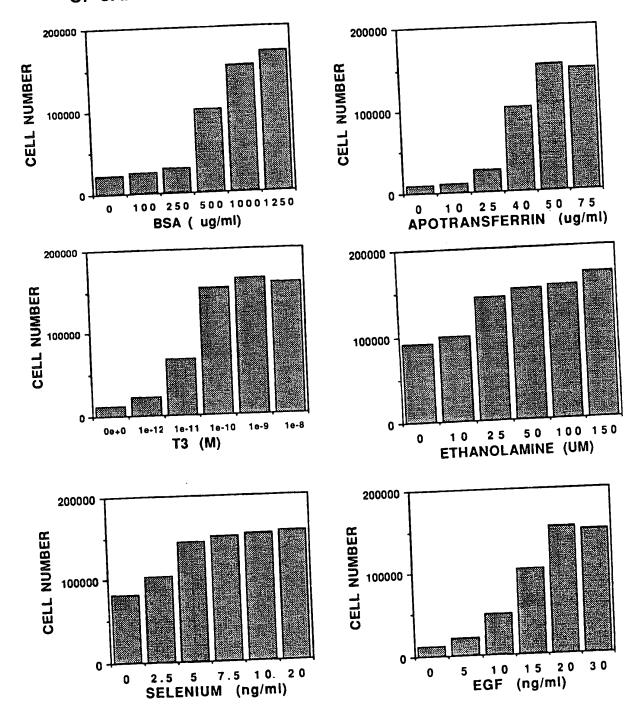
Hart the thirt

Hard there of the first that

į, į

FIGURE 34

DOSE-RESPONSE EFFECTS OF INDIVIDUAL COMPONENTS OF CAPM SERUM-FREE MEDIUM ON LNCAP CELL GROWTH



and the term of term of the term of te

Ē.

Express Mail EL818623436US

Inventor: Sirbasku

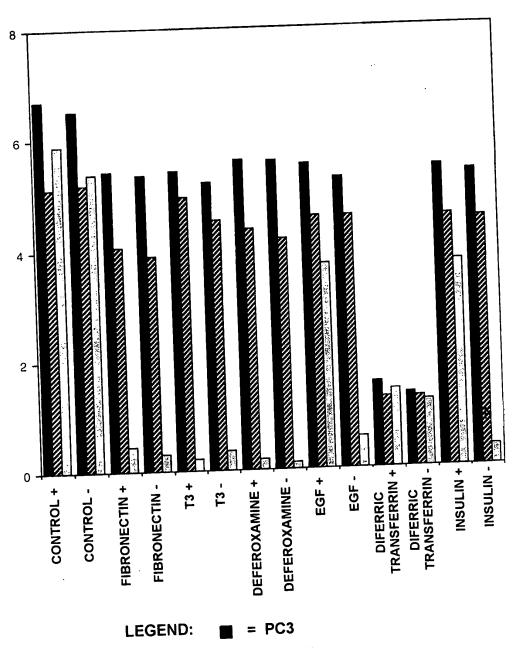
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 35 of 133

FIGURE 35

DELETIONS OF INDIVIDUAL COMPONENTS OF CAPM WITH PROSTATE CANCER CELL LINES



= DU145

🗔 = LNCaP

+ = 10 nM DHT

- = NO DHT

Inventor: Sirbasku

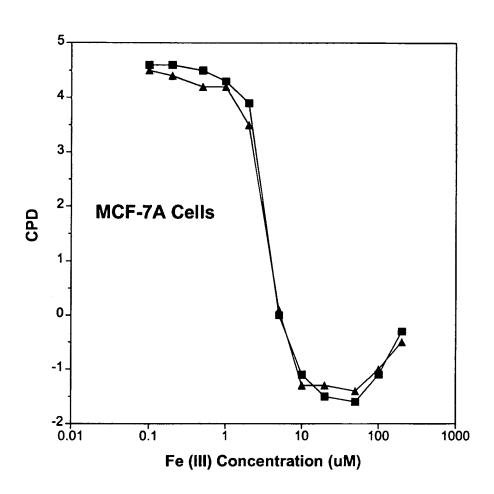
Atty Dkt. No. 1944-0080 **0**

Contact: C.G. Mintz (713) 238-8000

Page 36 of 133

FIGURE 36

EFFECT OF FE (III) IN MCF-7A CELL GROWTH IN DDM-2MF DEFINED MEDIUM



LEGEND:

plus E₂

 \longrightarrow minus E_2

Inventor: Sirbasku

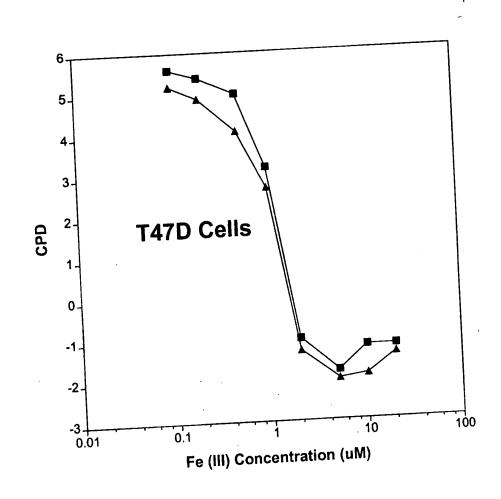
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 37 of 133

FIGURE 37

EFFECT OF FE (III) IN T47D CELL GROWTH IN DDM-2MF DEFINED MEDIUM



LEGEND:

plus E₂

minus E₂

ers person and green is a source term of a tree of the source of the sou

der der der Į, Sun and

Turb mult calle

i i Express Mail EL818623436US

Inventor: Sirbasku

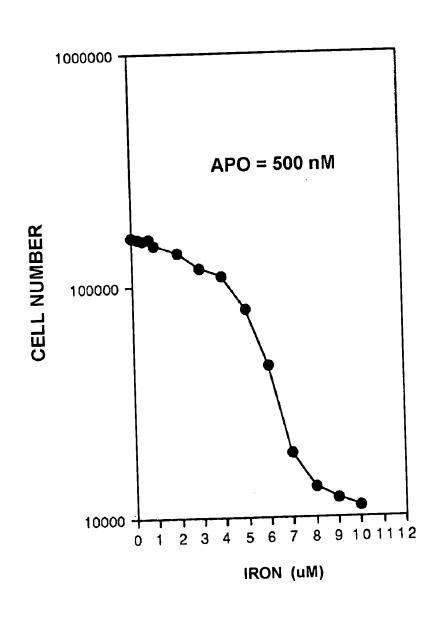
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 38 of 133

FIGURE 38

EFFECTS OF INCREASING CONCENTRATIONS OF IRON ON LNCaP CELLS GROWN IN SERUM-FREE MEDIUM WITH APOTRANSFERRIN



Inventor: Sirbasku

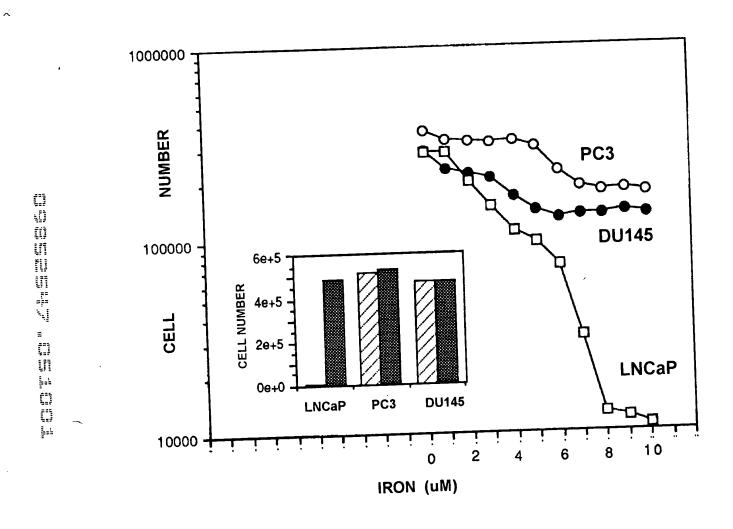
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 39 of 133

FIGURE 39

EFFECTS OF IRON AND T₃ ON THREE PROSTATIC CELL LINES IN SERUM-FREE MEDIUM



INSERT:

DARK BARS = GROWTH IN CAPM PLUS T_3 LIGHT (HATCHED) BARS = GROWTH IN CAPM MINUS T_3

NOTE THE STRIKING DEPENDENCE OF LNCaP CELLS ON $\,\mathrm{T}_3$

Inventor: Sirbasku

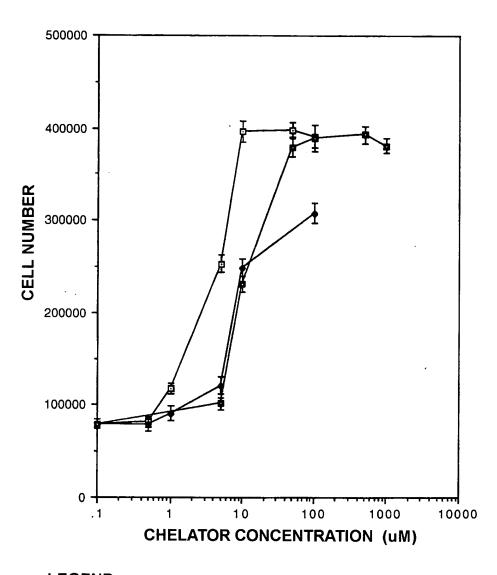
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 40 of 133

FIGURE 40

EFFECT OF CHELATORS ON SERUM-FREE T47D GROWTH UNDER HIGH IRON CONDITIONS



LEGEND:



Inventor: Sirbasku

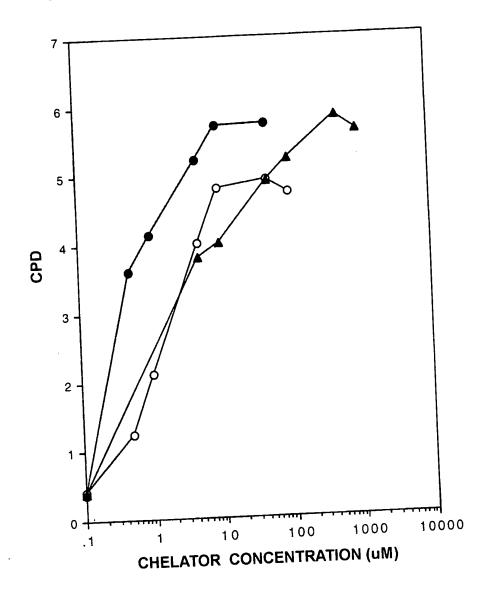
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 41 of 133

FIGURE 41

EFFECT OF CHELATORS ON SERUM-FREE LNCaP GROWTH UNDER HIGH IRON CONDITIONS



LEGEND:

Closed circles = Deferoxamine

Open circles = Citrate

Closed triangles = EDTA

And the second that the second second

Express Mail EL818623436US

Inventor: Sirbasku

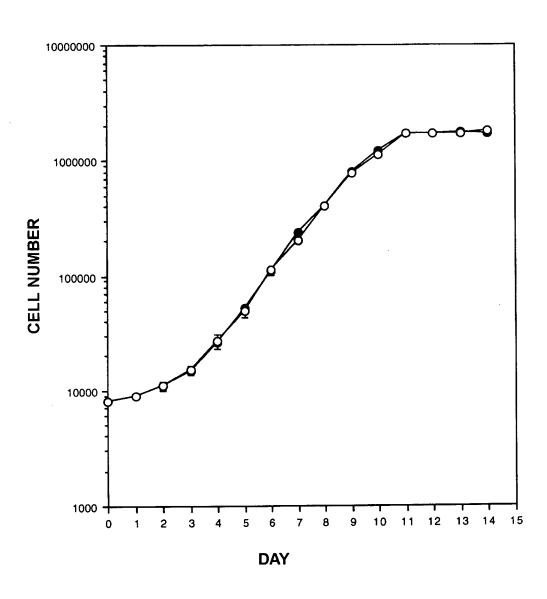
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 42 of 133

FIGURE 42

DU145 GROWTH IN SERUM-FREE MEDIUM BASED ON "LOW FE" OR "STANDARD" MEDIUM



LEGEND:

Open circles = "Low Fe" medium

Closed circles = "Standard" medium

Inventor: Sirbasku

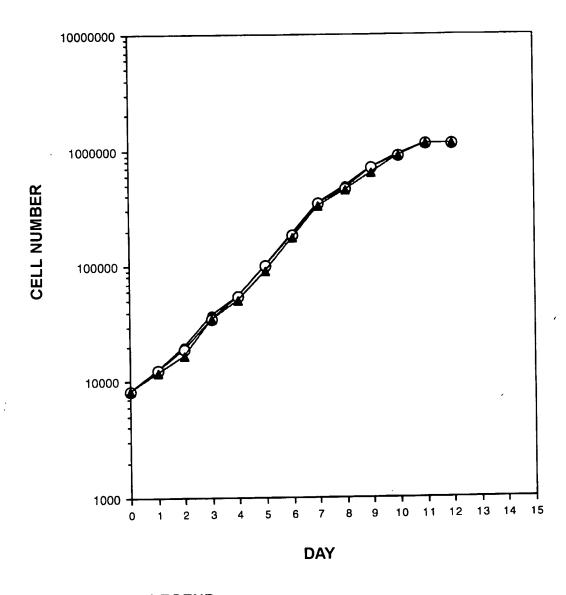
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 43 of 133

FIGURE 43

PC3 GROWTH IN SERUM-FREE MEDIUM BASED ON "LOW FE" OR "STANDARD" MEDIUM



LEGEND:

Harb dear ciet bross II is that had been Unit all had made

TI,

A THE STATE OF THE

1,1

aller that that aller aller

Open circles = "Low Fe" medium

Closed triangles = "Standard" medium

Inventor: Sirbasku

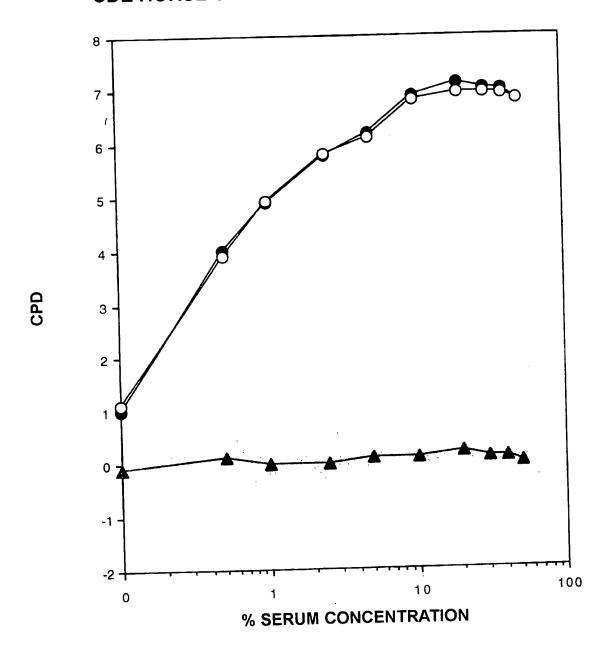
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 44 of 133

FIGURE 44

CDE HORSE SERUM TITRATION ON DU145 CELLS



LEGEND:

7.27 F 1.27 1.27

dealy them county them it is a secul

Dank thank than thank thank thanks

<u>.</u>...

---- = + 10 nM DHT

-O- = STEROID FREE

= ANDROGENIC EFFECT

Inventor: Sirbasku

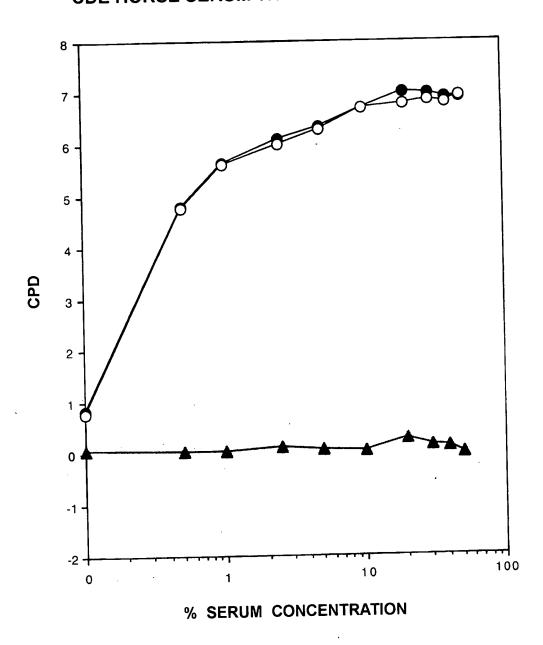
Atty Dkt. No. 1944-0080 **Q**

Contact: C.G. Mintz (713) 238-8000

Page 45 of 133

FIGURE 45

CDE HORSE SERUM TITRATION ON PC3 CELLS



LEGEND:

the first day have some than the state of the first state of the state

LII

###

ļ.i

—— = + 10 nM DHT

-O- = STEROID FREE

→ = ANDROGENIC EFFECT

Inventor: Sirbasku

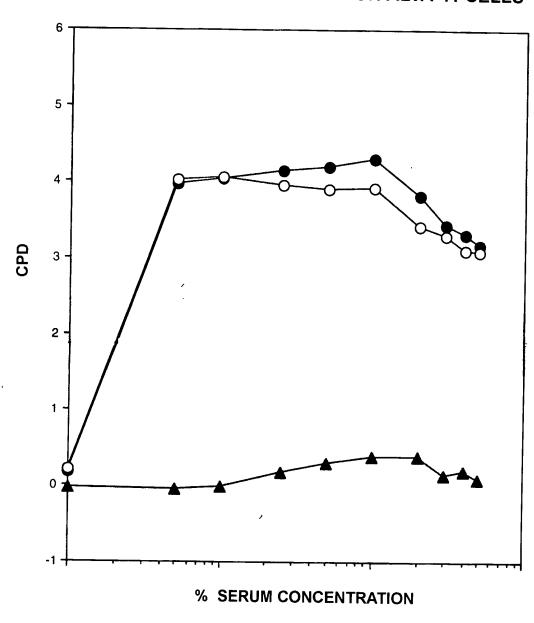
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 46 of 133

FIGURE 46

CDE HORSE SERUM TITRATION ON ALVA-41 CELLS



LEGEND:

-•- = + 10 nM DHT

--O-- = STEROID FREE

▲ = ANDROGENIC EFFECT

Inventor: Sirbasku

Atty Dkt. No. 1944-0080 **D**

Contact: C.G. Mintz (713) 238-8000

Page 47 of 133

107, 18 044, 107, 1878 4 18

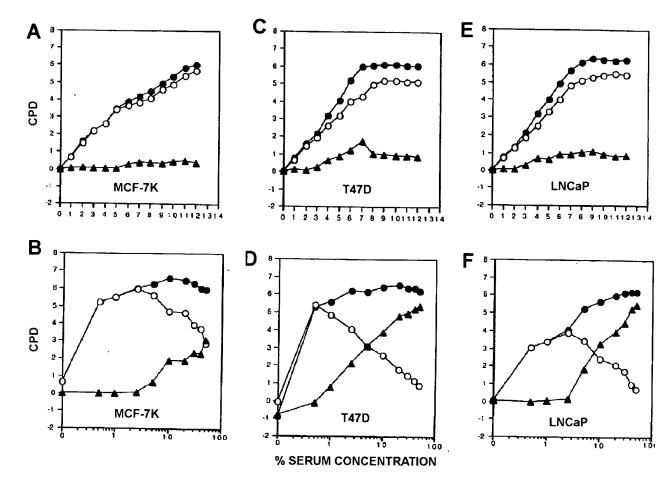
med form and then H. H. H. H. H. H.

171 1-1-

ģaš

FIGURE 47

EFFECTS OF ESTROGEN ON STEROID HORMONE-RESPONSIVE HUMAN TUMOR CELL GROWTH



The cells were grown in serum-free defined medium and in D-MEM/F-12 supplemented with increasing concentrations of CDE horse serum.

(A) MCF-7K cell growth was measured daily in serum-free defined DDM-2MF with 10 nM E_2 (closed circles) and without steroid (open circles) E_2 . Triangles = estrogenic effect. (B) MCF-7K cell growth measured after 12 d in D-MEM-F-12 supplemented with the designated concentrations of serum with E_2 (closed circles) and without steroid (open circles). The estrogenic effect is shown by triangles. (C) and (D) show the same experiments as in (A) and (B), respectively, except with T47D cells. (E) and (F) show the same experiments as in (A) and (B), respectively, xcept with LNCaP cells. In (E) the serum-free medium was CAPM.

Inventor: Sirbasku

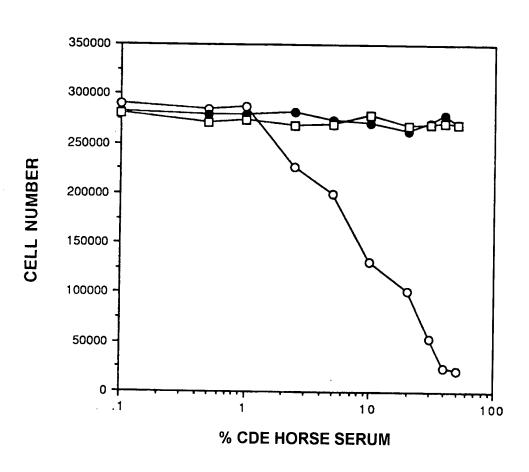
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 48 of 133

FIGURE 48

CDE HORSE SERUM TITRATION ON LNCaP GROWTH IN SERUM FREE CONDITIONS



LEGEND:

. Article from the first that the first first first the first firs

Ĕ=h

Express Mail EL818623436US

Inventor: Sirbasku

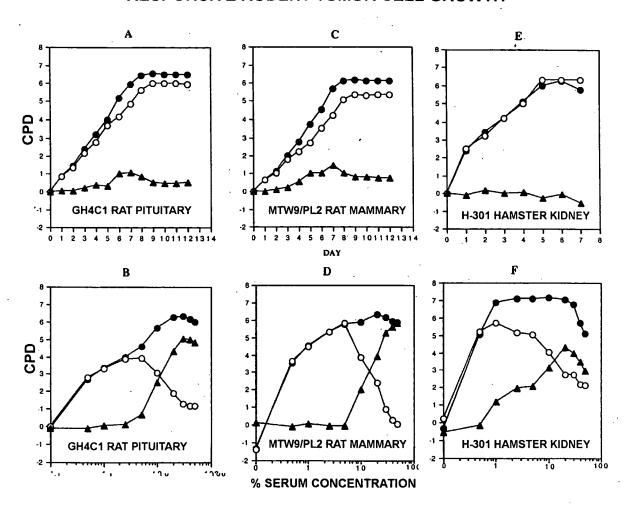
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 49 of 133

FIGURE 49

EFFECTS OF ESTROGEN ON STEROID HORMONE-RESPONSIVE RODENT TUMOR CELL GROWTH



Comparison of the effects of estrogen on steroid hormone-responsive rodent tumor cell growth in serum-free defined medium and in D-MEM/F-12 supplemented with increasing concentrations of CDE horse serum.

(A) GH_4C_1 rat pituitary tumor cell growth measured daily in serum-free PCM-9 with E_2 (closed circles) and without E_2 (open circles). The estrogenic effect is shown by triangles. (B) GH_4 C_1 cell growth measured after 9 d in D-MEM-F-12 supplemented with the designated concentrations of CDE horse serum with E_2 (closed circles) and without E_2 (open circles). The estrogenic effect is shown by triangles. (C) and (D) show the same experiments as in (A) and (B) respectively, but with th MTW9/PL2 rat mammary tumor cells. The serum-free medium in (D) was DDM-2A. (E) and (F) show the same experiments as in (A) and (B), respectively, except with the H-301 hamster kidney tumor cells. In (E) the serum-free medium was CAPM.

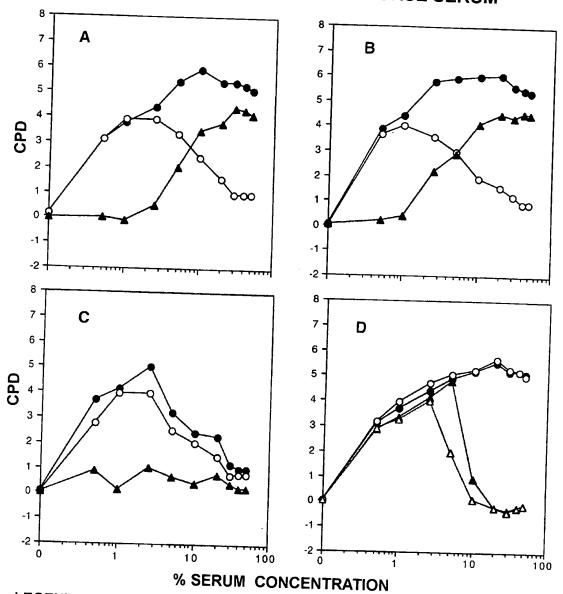
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 50 of 133

FIGURE 50

THE EFFECT OF DHT, $\,\mathrm{E}_{2}^{}$, AND DES ON LNCap CELLS GROWN IN CDE HORSE SERUM



LEGEND:

- (A) Open circles = DHT Closed circles = + DHT Closed trianges = Androgenic effect
- (B) Open circles = -E₂ Closed circles = $+E_2$ Closed triangles = Estrogenic eff ct
- (C) Open circles = DES Closed circles = + DES Closed triangles = Estrogenic effect
- (D) Open circles = DHT & DES Closed circles = E_2 & DES Open triangles = No additions Closed triangles = DES only

Inventor: Sirbasku

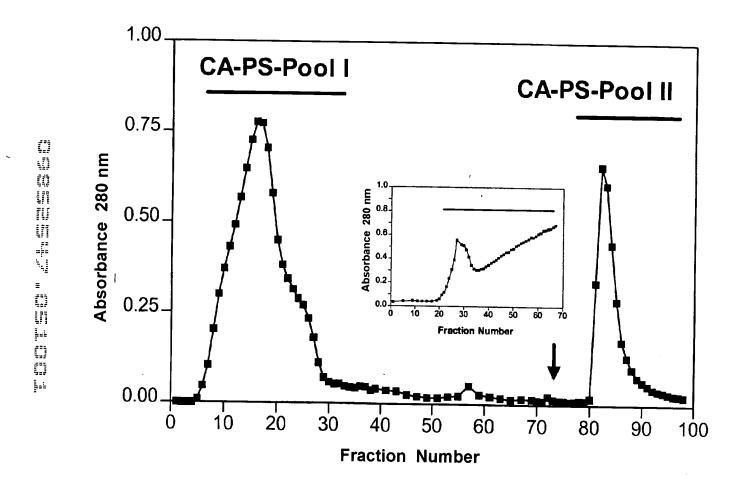
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 51 of 133

FIGURE 51

PHENYL SEPHAROSE ELUTION OF CBG (CA-PS-POOL 1) AND SHBG-LIKE (CA-PS-POOL 11)



ARROW = ELUTION WITH 40% ETHYLENE GLYCOL

INSERT: CORTISOL AFFINITY COLUMN ELUTION

BARS = POOLED ACTIVE FRACTION

Inventor: Sirbasku

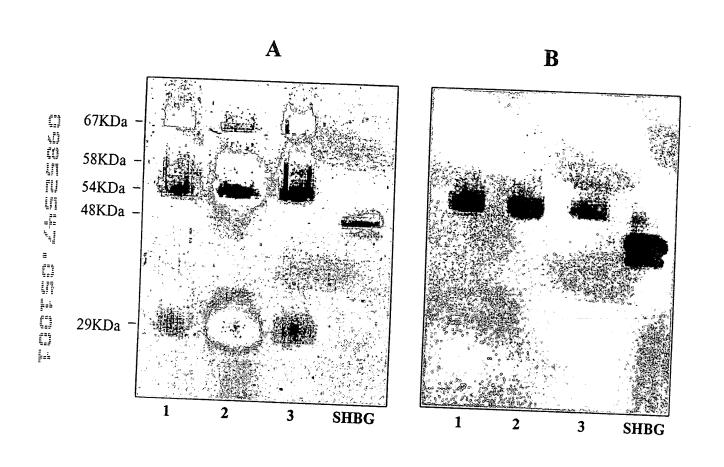
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 52 of 133

FIGURE 52

SDS PAGE (A) AND WESTERN ANALYSIS (B) OF THREE PREPARATIONS OF CA-PS-POOL II VS HUMAN SHBG



LANES 1, 2, AND 3 = 10 ug each of CA-PS-POOL II LANE "SHBG" = 10 mg of purified protein

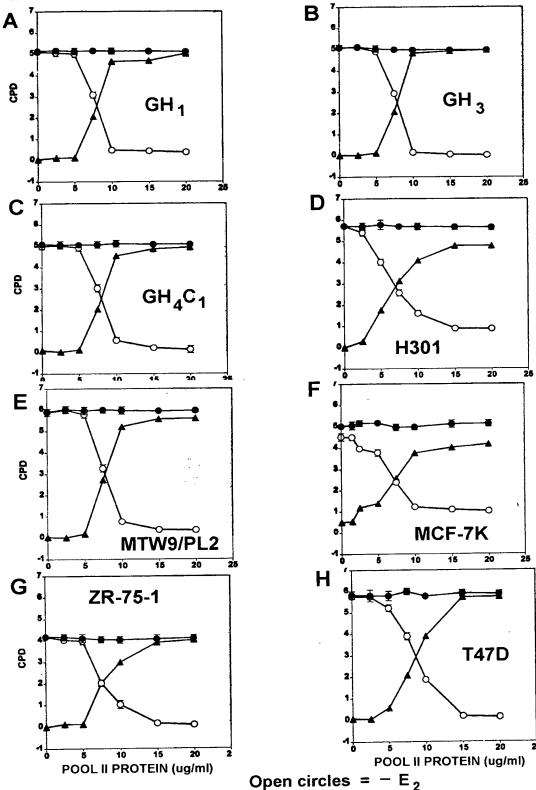
Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 53 of 133

FIGURE 53

ASSAY OF CA-PS-POOL II ESTROGEN REVERSIBLE INHIBITORY ACTIVITY WITH SEVERAL ER*CELL LINES



LEGEND:

Clos d circles = $+ E_2$

Closed triangl s = Estrog nic effect

Inventor: Sirbasku

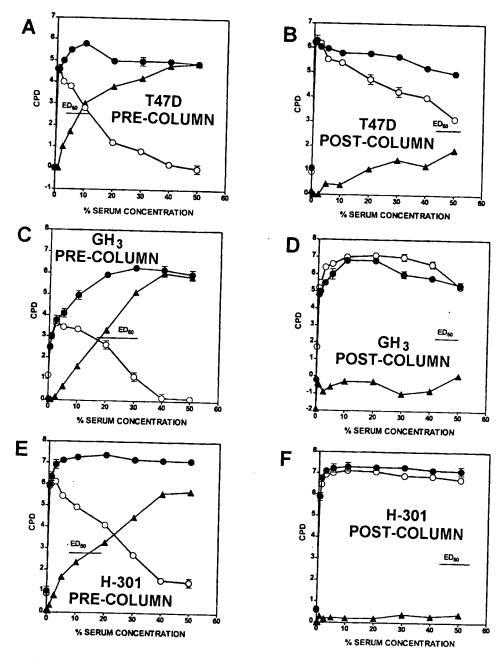
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 54 of 133

FIGURE 54

CORTISOL-AGAROSE AFFINITY REMOVAL OF THE INHIBITOR FROM CDE-SERUM



LEGEND:

Open circles = $-E_2$

Closed circl s = + E₂

Closed triangles = Estrogenic effect

ļ.

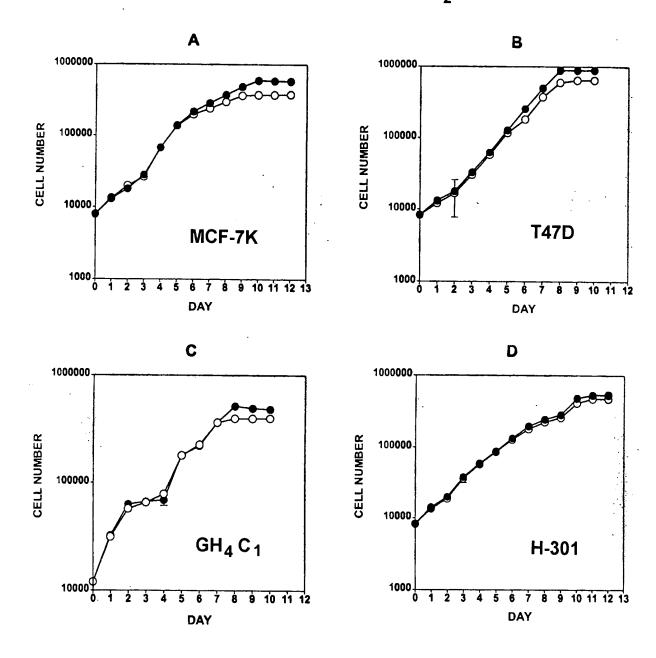
Atty Dkt. No. 1944-0080 v

Contact: C.G. Mintz (713) 238-8000

Page 55 of 133

FIGURE 55

GROWTH OF ER + CELL LINES IN SERUM-FREE MEDIUM ± E₂



LEGEND:

[]

the speak gives made there is a seed to the seed to th

The france of

Closed circles =
$$+ E_2$$

Open circles = $- E_2$

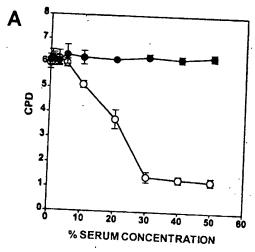
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

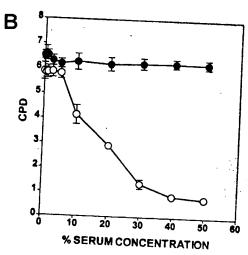
Page 56 of 133

FIGURE 56

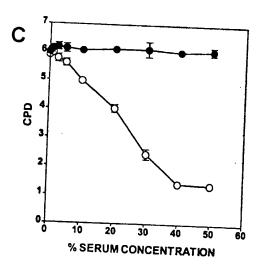
EFFECT OF CDE-SERUM ON ESTROGEN RESPONSIVE GROWTH OF THREE ER+ CANCER CELL LINES IN SFM



T47D IN DDM-2MF



B = MTW9/PL2 IN DDM-2A



C =GH₄ C₁ IN PCM 9

Inventor: Sirbasku

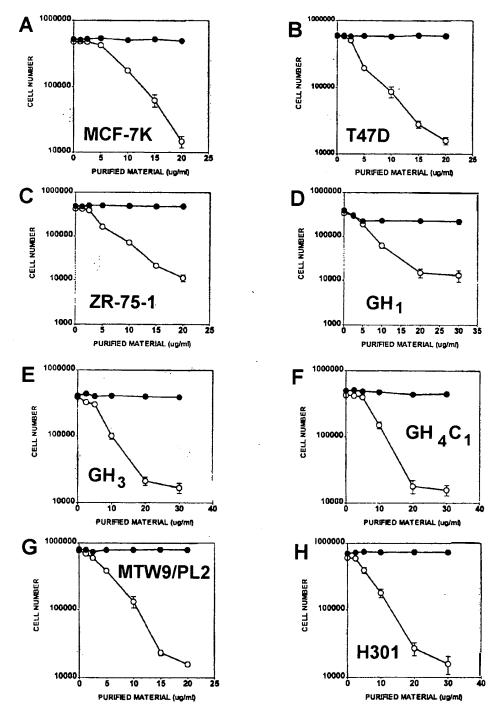
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 57 of 133

FIGURE 57

EFFECT OF CA-PS-POOL II ON ESTROGEN RESPONSIVE GROWTH IN SERUM FREE MEDIUM



LEGEND: Open circles = $-E_2$ Closed circles = $+E_2$

 Express Mail EL818623436US

Inventor: Sirbasku

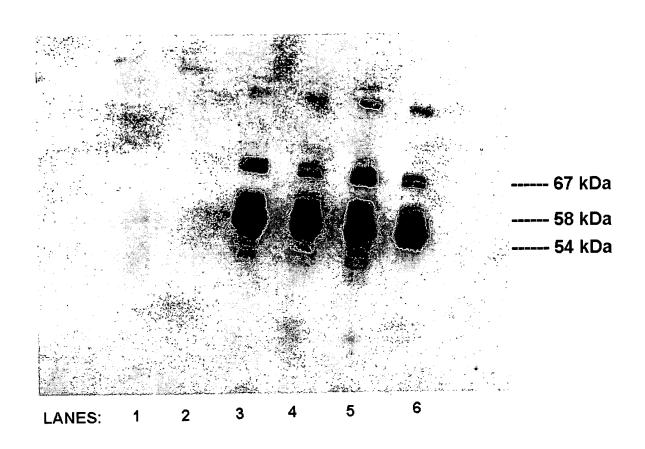
Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 58 of 133

FIGURE 58

WESTERN ANALYSIS OF CBG (POOL I) AND SHBG (POOL II) PREPARATION WITH ANTI-54 kDa



1 = CBG PREPARATION #5

2 = CBG PREPARATION #6

3 = SHBG PREPARATION #5.1

4 = SHBG PREPARATION #5.2

5 = SHBG PREPARATION #6.1

6 = SHBG PREPARATION #6.2

ANTIBODY = RABBIT ANTI-54 kDa 1:5000 DILUTION

Inventor: Sirbasku

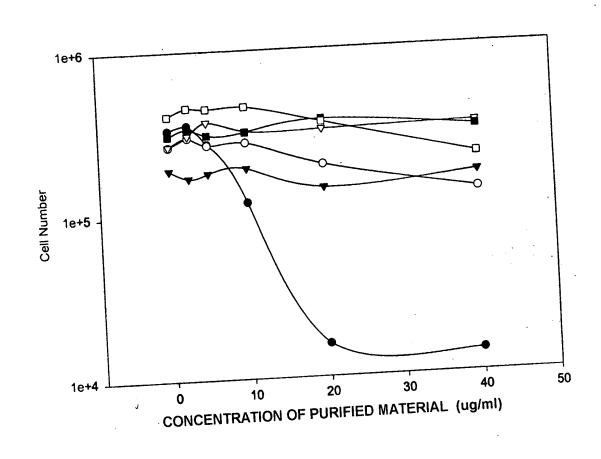
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 59 of 133

FIGURE 59

EFFECT OF ANTI-54kDa ANTISERUM ON MTW9/PL2 CELLS GROWN IN THE PRESENCE OF CA-PS-POOL II



100 Mar. destroy there may been the result that the district that the distr Hart mail FaF

> No antibody LEGEND:

-->- Antibody 1:5000

Antibody 1:1000

-√- Antibody 1:500

–■ Antibody 1:100

-D- Antibody 1:50

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

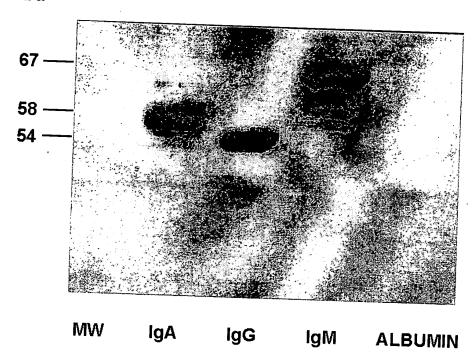
Contact: C.G. Mintz (713) 238-8000

Page 60 of 133

FIGURE 60

WESTERN BLOT OF COMMERCIAL PREPARATIONS OF HORSE IGA, IGG AND IGM WITH THE ANTI-54 kDa ANTIBODY

MkDa



Anny Array (and person and person and the second array (and the se

F.,

ļ.b

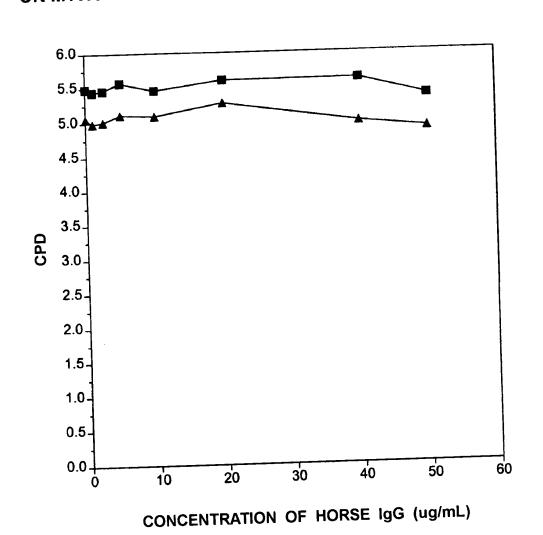
Express Mail EL818623436US Inventor: Sirbasku Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 61 of 133

FIGURE 61

EFFECT OF COMMERCIALLY PURIFIED HORSE IgG ON MTW9/PL2 CELL GROWTH IN 2.5% CDE-HORSE SERUM



LEGEND: - plus E_2 - minus E_2

Inventor: Sirbasku

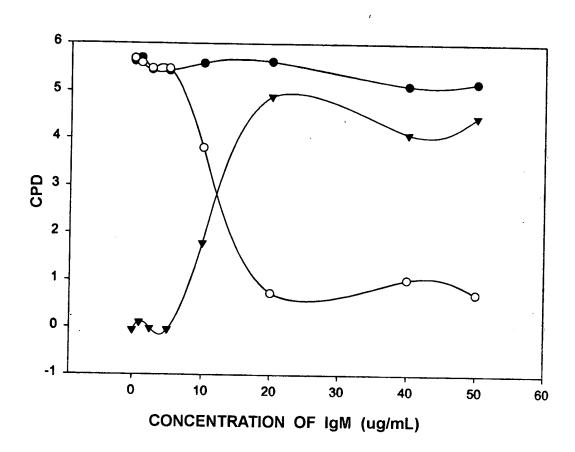
Atty Dkt. No. 1944-0080 **0**

Contact: C.G. Mintz (713) 238-8000

Page 62 of 133

FIGURE 62

EFFECT OF HORSE IgM ON GROWTH OF THE MTW9/PL2 CELLS IN 2.5% CDE HORSE SERUM \pm E $_2$



the death forms could be seen that the seen

LEGEND:

= Estrogenic effect

Inventor: Sirbasku

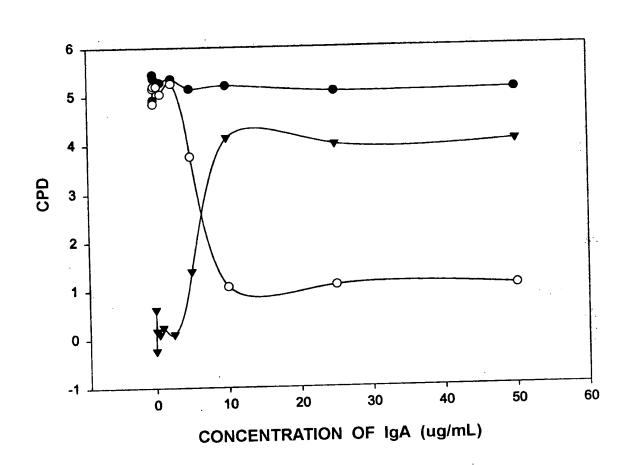
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 63 of 133

FIGURE 63

EFFECT OF HORSE IgA ON GROWTH OF THE MTW9/PL2 CELLS IN 2.5% CDE HORSE SERUM $\pm\,\mathrm{E}_{\,2}$



LEGEND:

The first proof that the from the first to t

Liventor: Sirbacku

Atty Dkt. No. 1944-00800

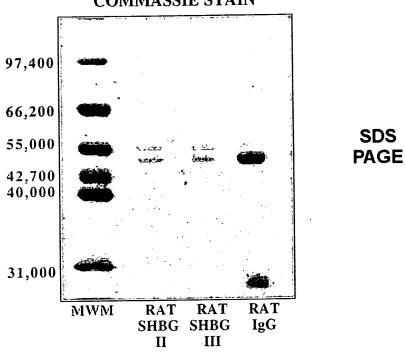
Contact: C.G. Mintz (713) 238-80

Page 64 of 133

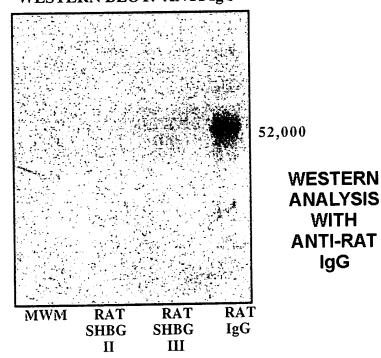
FIGURE 64

SDS PAGE AND WESTERN ANALYSIS OF RAT "SHBG-LIKE" PREPARATIONS

COMMASSIE STAIN



WESTERN BLOT. ANTI IgG



Express Mail EL618023430CS

inventor: Sirbasku

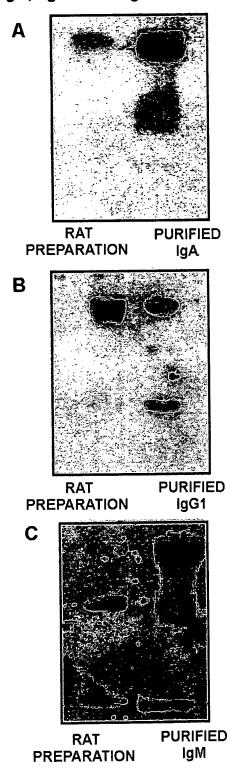
Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 65 of 133

FIGURE 65

CROSSREACTION OF THE PURIFIED RAT "SHBG-LIKE" PROTEINS WITH ANTI- IgA, IgG1 AND IgM MONOCLONAL ANTIBODIES



Inventor: Sirhaskii Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 66 of 133

[]

H.

111

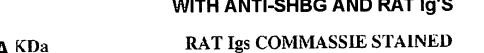
thus word H .f"

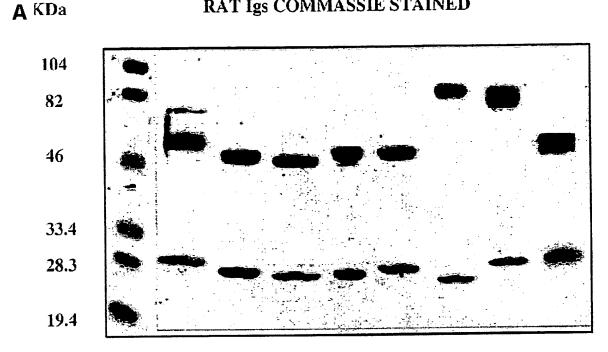
ĩ)

12

FIGURE 66

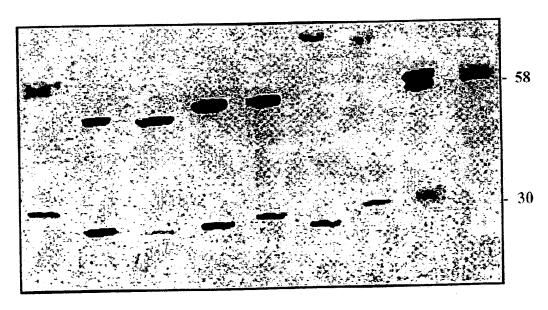
SDS PAGE (A) AND WESTERN ANALYSIS (B) WITH ANTI-SHBG AND RAT Ig'S





MW IgA IgG1 IgG2a IgG2b IgG2c IgE IgM RP

B RAT Igs WESTERN BLOT. ANTI SHBG ANTIBODY KDa



lgA lgG1 lgG2a lgG2b lgG2c lgE lgM HP RP

Inventor: Sirbasku

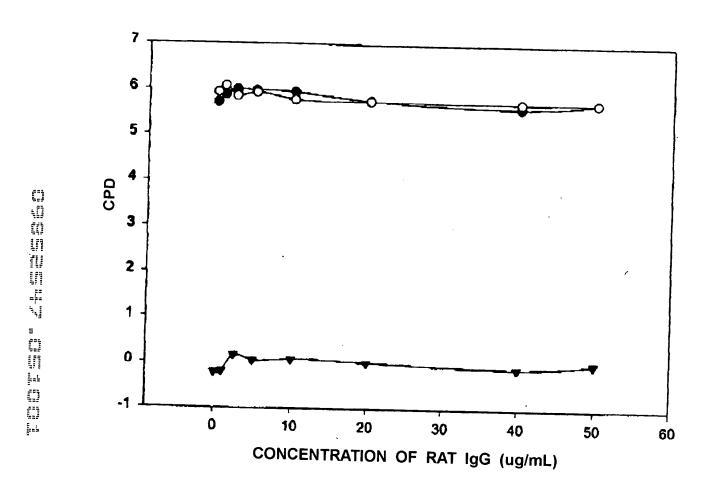
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 67 of 133

FIGURE 67

EFFECT OF RAT IgG ON MTW9/PL2 CELL GROWTH IN 2.5% CDE RAT SERUM



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Closed triangles = Estrogenic effect

Inventor: Sirbasku

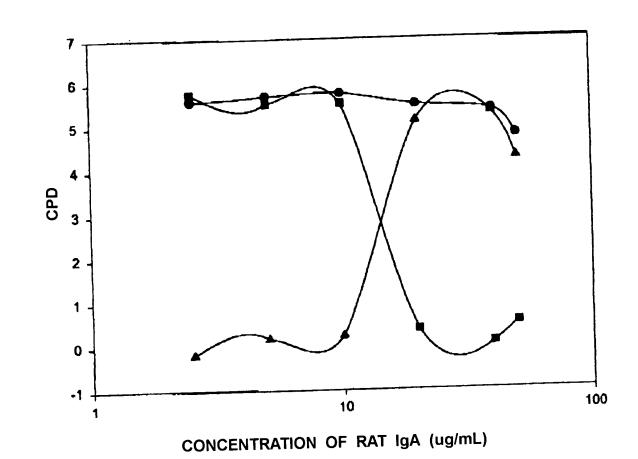
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 68 of 133

FIGURE 68

EFFECT OF RAT IGA ON MTW9/PL2 CELL GROWTH IN 2.5% CDE RAT SERUM



LEGEND:

dust the free mind their cost than the sent that it

the fact that

ļ.

Closed circles = $+ E_2$

Closed squares = $-E_2$

Closed triangles = Estrogenic effect

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

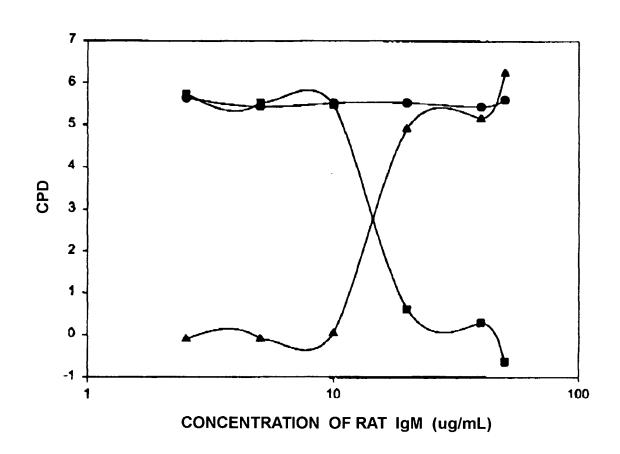
Contact: C.G. Mintz (713) 238-8000

Page 69 of 133

FIGURE 69

EFFECT OF RAT IgM ON MTW9/PL2 CELL

GROWTH IN 2.5% CDE RAT SERUM



LEGEND:

47

[] []

Ban mad B.

إ

that that the

The following the state of the

Closed squares = $-E_2$

Closed circles = $+ E_2$

Closed triangles = Estrogenic effect

Inventor: Sirbasku

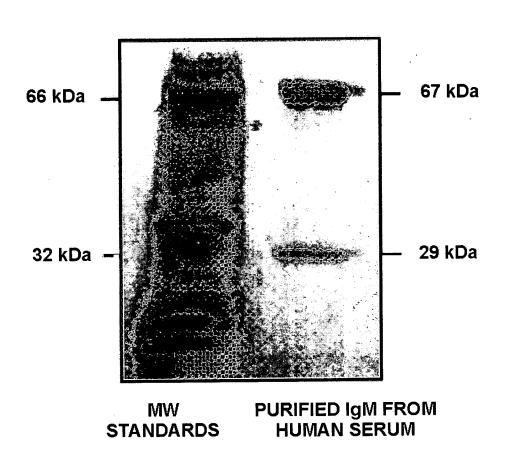
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 70 of 133

FIGURE 70

ELUTION OF IGM FROM MANNAN BINDING PROTEIN COLUMN



Express Mail EL818623436US Inventor: Sirbasku

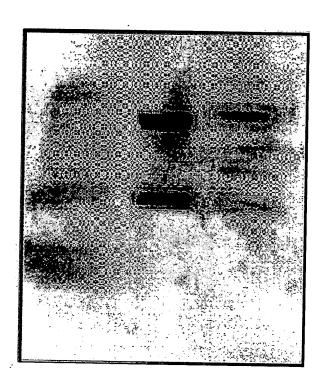
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 71 of 133

FIGURE 71

IgM PURIFICATION FROM **PLASMA BY JACALIN**



MW **HUMAN PURIFIED** lgA **IgA**

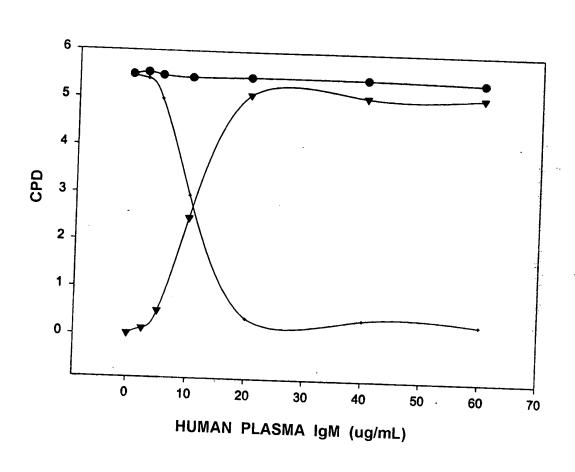
Express Mail EL818623436US Inventor: Sirbasku

Atty Dkt. No. 1944-0080 **0** Contact: C.G. Mintz (713) 238-8000

Page 72 of 133

FIGURE 72

EFFECT OF IgM ISOLATED FROM HUMAN PLASMA ON MTW9/PL2 GROWTH IN SERUM-FREE CONDITIONS



girth girth girth teach trong passe p g many grown the base of the g of the grown and then small the g of the grown that g of the g of the

.

LEGEND:

= Estrogenic effect

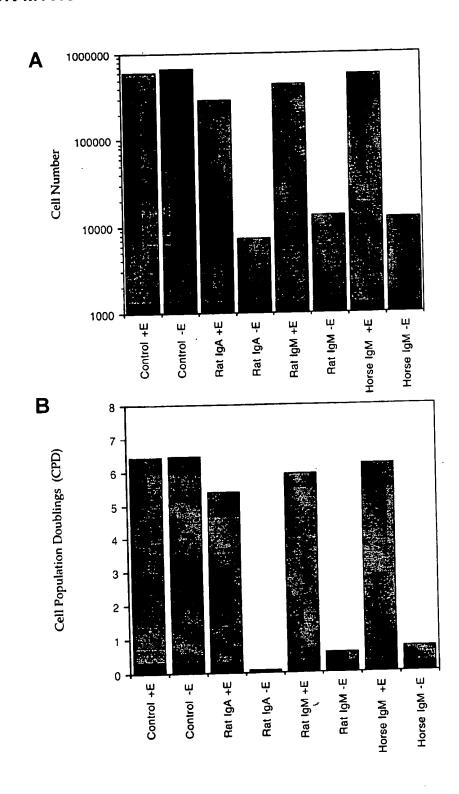
Inventor: Sirbasku

Atty Dkt. No. 1944-0080**0** Contact: C.G. Mintz (713) 238-8000

Page 73 of 133

FIGURE 73

THE EFFECT OF VARIOUS IGA AND IGM PREPARATIONS ON MTW9/PL2 CELLS GROWN IN SERUM-FREE MEDIUM



Inventor: Sirbasku

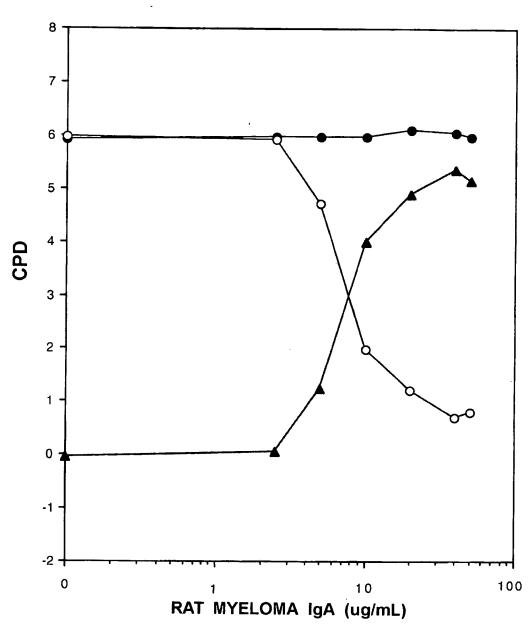
Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 74 of 133

FIGURE 74

RAT MYELOMA IGA TITRATION ON GH₁ CELLS GROWN IN SERUM-FREE CONDITIONS



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Closed triangles = Estrogenic effect

É

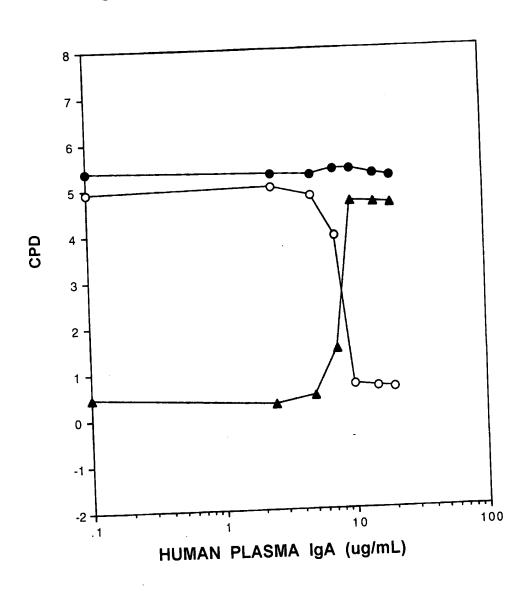
Inventor: Sirbasku

Atty Dkt. No. 1944-00800 Contact: C.G. Mintz (713) 238-8000

Page 75 of 133

FIGURE 75

HUMAN PLASMA IGA TITRATION ON GH₁ CELLS **GROWN IN SERUM-FREE CONDITIONS**



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Inventor: Sirbasku

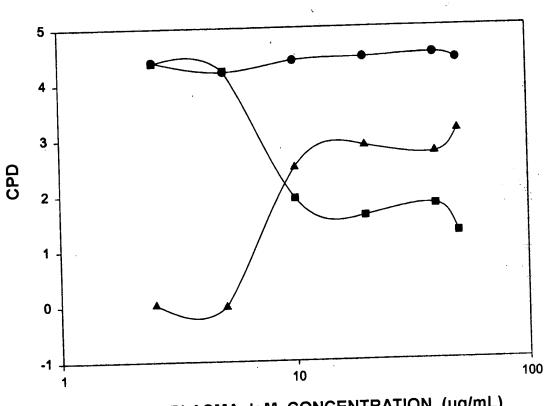
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 76 of 133

FIGURE 76

HUMAN PLASMA IGM TITRATION ON GH₁ CELLS GROWN IN SERUM-FREE CONDITIONS



HUMAN PLASMA IGM CONCENTRATION (ug/mL)

LEGEND:

the state does done there work there there is need the state of the st

4.... m....

Express Mail EL81802343000 Inventor: Sirbasku

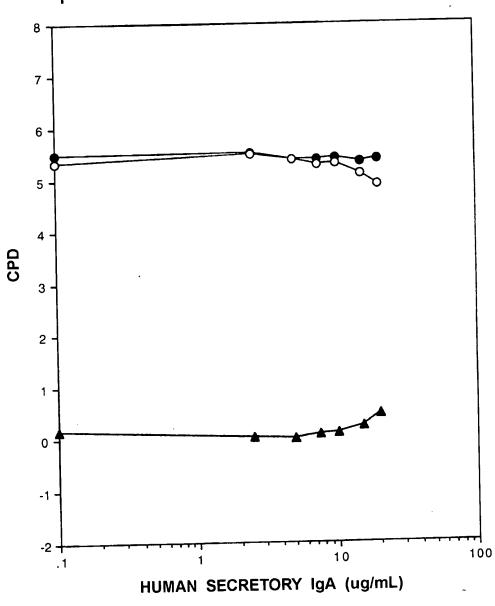
Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 77 of 133

FIGURE 77

EFFECT OF HUMAN SECRETORY IGA ON GH₁ CELLS GROWN IN SERUM-FREE CONDITIONS



LEGEND:

Closed circles = $+E_2$

Open circles = $-E_2$

Inventor: Sirbasku

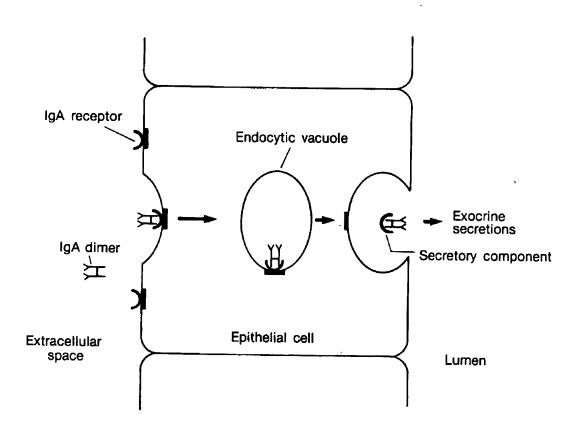
Atty Dkt. No. 1944-00807

Contact: C.G. Mintz (713) 238-8000

Page 78 of 133

FIGURE 78

MECHANISM OF TRANSCYTOSIS OF IGA AND IGM BY MUCOSAL EPITHELIAL CELLS



Inventor: Sirbasku

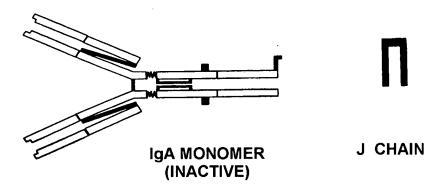
Atty Dkt. No. 1944-00800

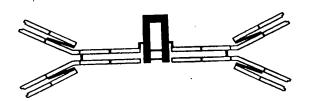
Contact: C.G. Mintz (713) 238-8000

Page 79 of 133

FIGURE 79

ESSENTIAL STRUCTURES OF HUMAN PLASMA AND SECRETORY IGA







IgA DIMER WITH ATTACHED J CHAIN (ACTIVE)

SECRETORY PIECE OR SECRETORY COMPONENT (80% POLY-IgR)



SECRETORY IGA SHOWING J CHAIN AND SECRETORY COMPONENT (INACTIVE)

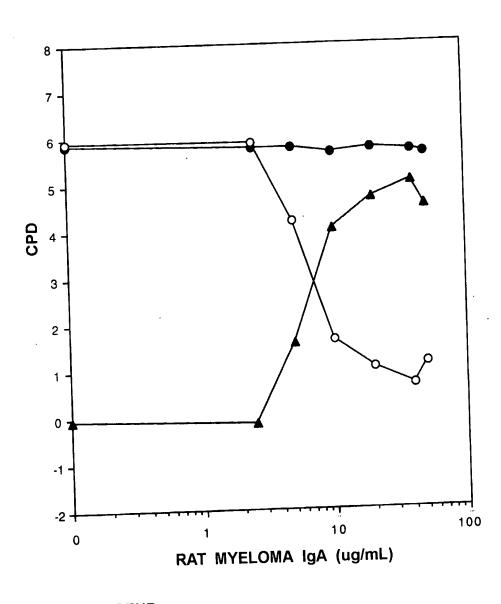
Inventor. Subasku Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 80 of 133

FIGURE 80

EFFECT OF RAT MYELOMA IGA ON GH $_{\rm 3}$ CELLS GROWN IN SERUM-FREE MEDIUM



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

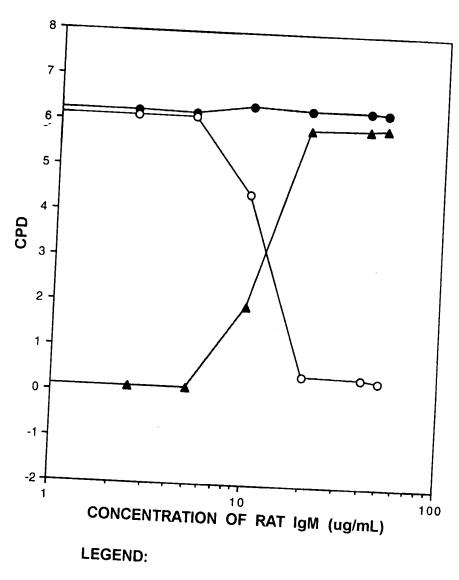
Inventor: Sirbasku Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 81 of 133

FIGURE 81

EFFECT OF RAT IGM ON GH_3 CELL GROWTH IN SERUM-FREE MEDIUM



= Estrogenic effect

n en gerin gerin term men, grow it a reerg grow to grow all grows at grows and the state of the

£.) ŧ[] Ü M 74 [] IJ

> ļ.

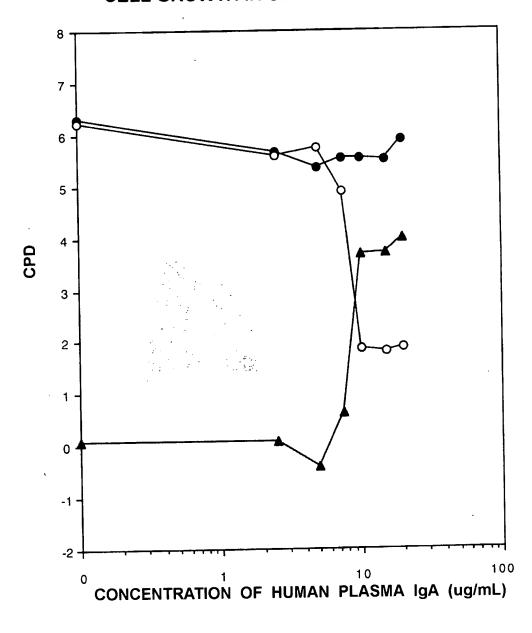
Express Mail EL61602343003

Inventor: Sirbasku

Atty Dkt. No. 1944-00800 Contact: C.G. Mintz (713) 238-8000

Page 82 of 133

FIGURE 82 EFFECT OF HUMAN PLASMA IgA ON GH₃ **CELL GROWTH IN SERUM-FREE MEDIUM**



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

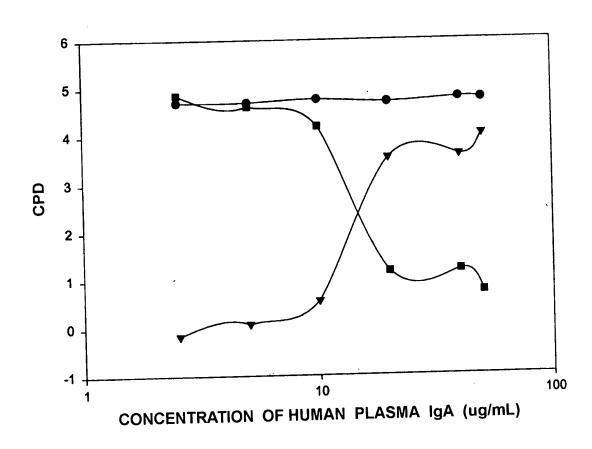
Inventor: Eirbacku Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 83 of 133

FIGURE 83

EFFECT OF HUMAN PLASMA IGM ON GH $_{\rm 3}$ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

7

the transmit the state of the transmit the state of the s

Inventor: Sirbasku

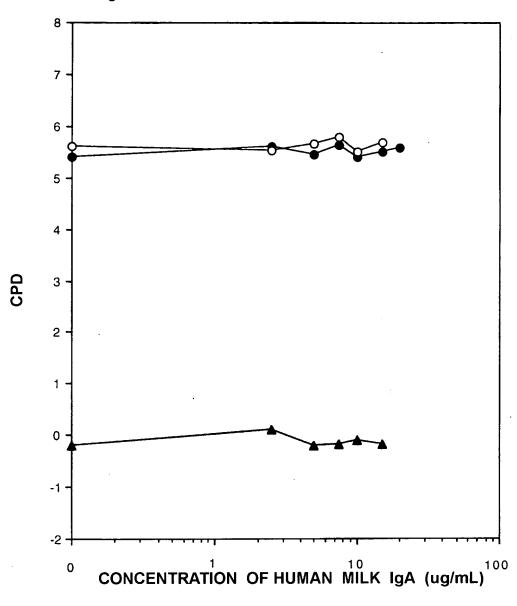
Atty Dkt. No. 1944-00807

Contact: C.G. Mintz (713) 238-8000

Page 84 of 133

FIGURE 84

EFFECT OF HUMAN MILK SECRETORY IGA ON GH₃ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Express Mail CL018623436LIS

Inventor: Sirbasku

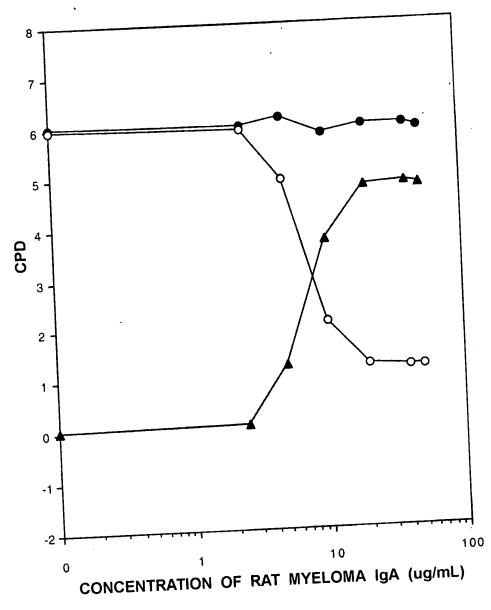
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 85 of 133

FIGURE 85

EFFECT OF RAT MYELOMA IGA ON GH_4 CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

den trans dear des constitues trans transfer transf

they again from and they they

Closed circles = $+ E_2$

Open circles = - E₂

Express Mail EL818623436US

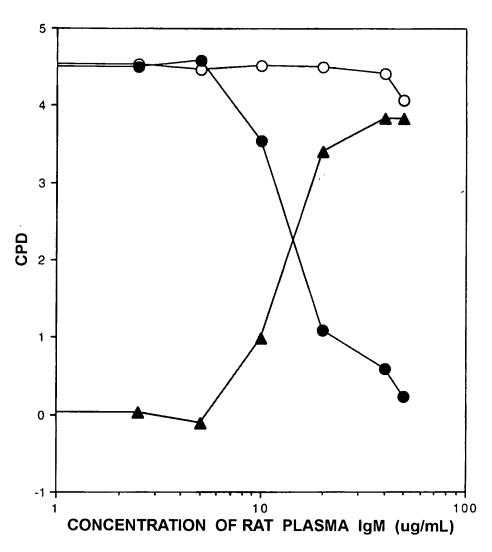
Inventor: Sirbasku Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 86 of 133

FIGURE 86

EFFECT OF RAT PLASMA IgM ON GH₄ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

$$-\bigcirc - = + E_2$$

—<u>▲</u> = Estrogenic effect

Inventor: Sirbasku

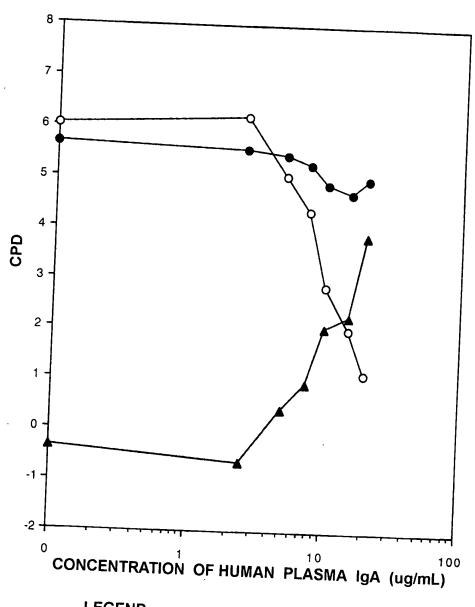
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 87 of 133

FIGURE 87

EFFECT OF HUMAN PLASMA IGA ON GH $_4$ C $_1$ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Express Mail EL81802343003 Inventor: Sırbasku

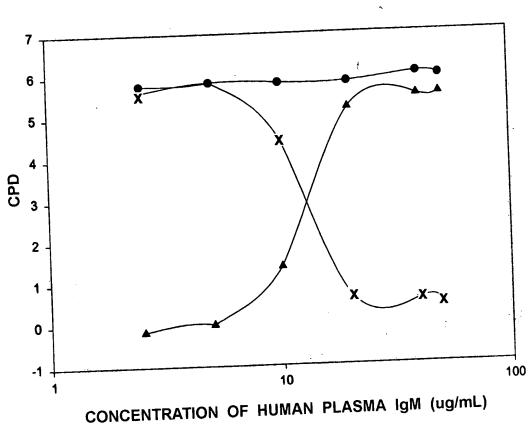
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 88 of 133

FIGURE 88

EFFECT OF HUMAN PLASMA IGM ON GH₄C₁ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

$$-x-=-E_2$$

= Estrogenic effect

the first and then were their a sort the the transmission of transmission of the transmission of the transmission of transm

Inventor: Sirbasku

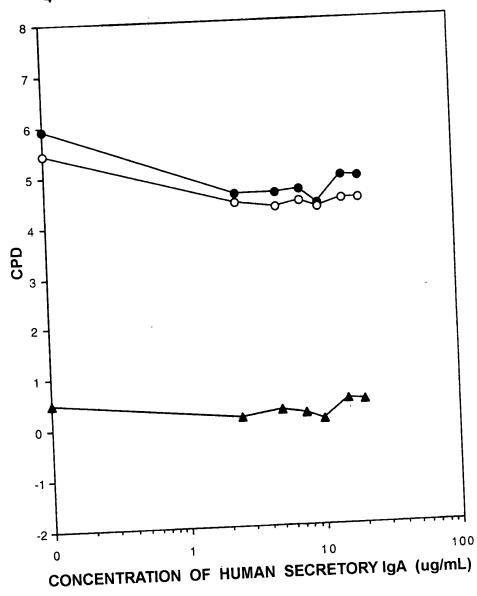
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 89 of 133

FIGURE 89

EFFECT OF HUMAN MILK SECRETORY IGA ON $\mathrm{GH_4C_1}$ CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Closed triangles = Estrogenic effect

der the state of t

i Esi Inventor: Sirbasku Atty Dkt. No. 1944-00807

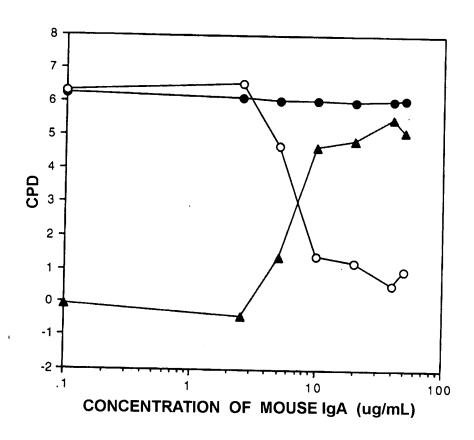
Contact: C.G. Mintz (713) 238-8000

Express Mail EL818623436LIS

Page 90 of 133

FIGURE 90

EFFECT OF MOUSE IgA ON H301 CELL **GROWTH IN SERUM-FREE MEDIUM**



LEGEND:

Closed circles = $+ E_2$

Open circles = $-E_2$

Express Mail ELS (8023-3000

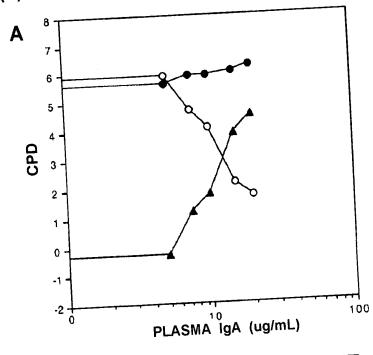
Atty Dkt. No. 1944-00800

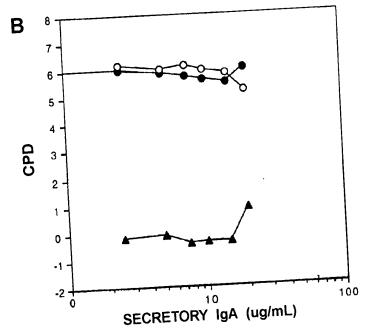
Contact: C.G. Mintz (713) 238-8000

Page 91 of 133

FIGURE 91

EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IgA (B) ON H301CELL GROWTH IN SERUM-FREE MEDIUM





Clos d circles = $+ E_2$ LEGEND: Open circles = - E₂

Closed triangles = Estrogenic effect

Inventor: Sırbasku

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 92 of 133

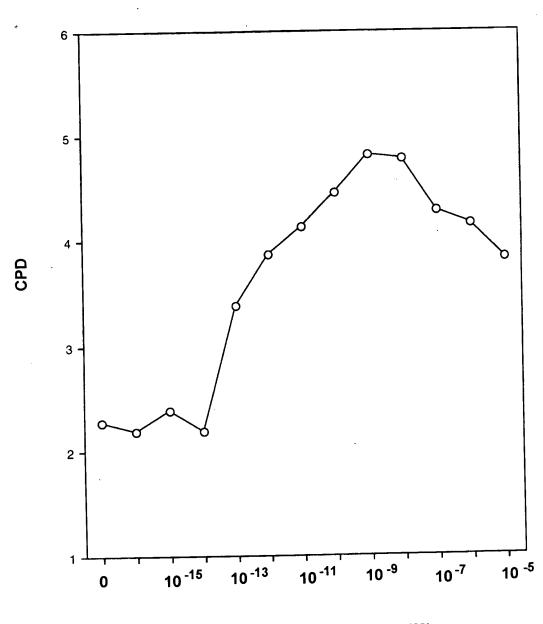
The transfer

11

Territ of the House State

FIGURE 92

EFFECT OF ESTRADIOL ON H301 CELL GROWTH IN SERUM-FREE MEDIUM AND 40 ug/mL OF HUMAN IgM



ESTRADIOL CONCENTRATION (M)

death death court prior seast the level of the death court of the deat

Express Mail EL818623436US

Inventor: Sirbasku

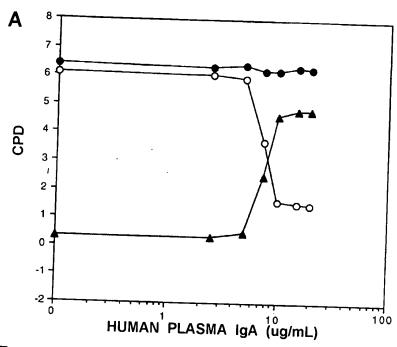
Atty Dkt. No. 1944-00800

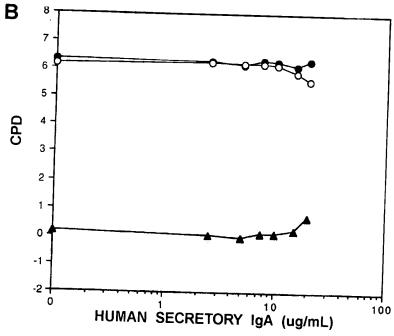
Contact: C.G. Mintz (713) 238-8000

Page 93 of 133

FIGURE 93

EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IGA (B) ON MCF-7K CELL GROWTH IN SERUM-FREE MEDIUM





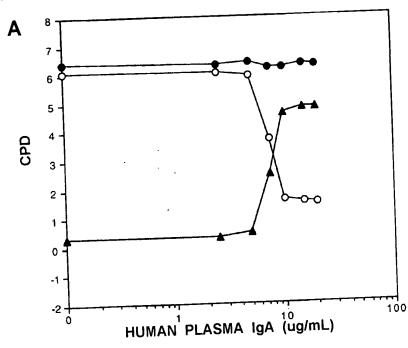
LEGEND: Closed circles = + E₂
Open circles = - E₂
Closed triangles = Estrogenic effect

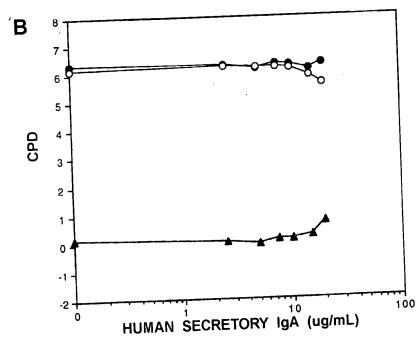
Inventor: Sirbasku y Dkt. No. 1944-0080**0**

ontact: C.G. Mintz (713) 238-8000

Page 94 of 133

FIGURE 94 EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IGA (B) ON MCF-7KCELL GROWTH IN SERUM-FREE MEDIUM





Closed circles = $+ E_2$ LEGEND: Open circles = $-E_2$

Inventor: Sirbasku

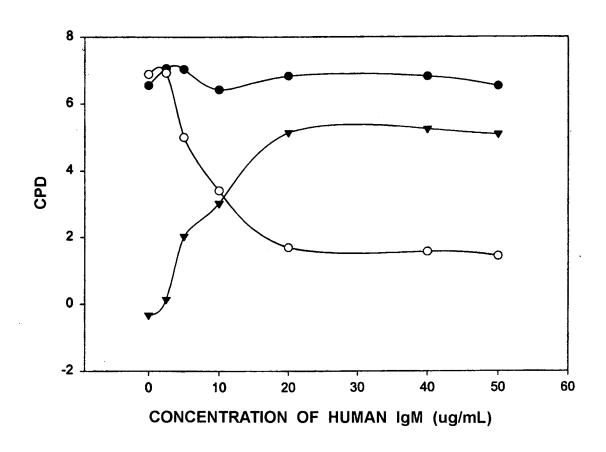
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 95 of 133

FIGURE 95

EFFECT OF HUMAN IgM ON MCF-7A CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

$$- - = - E_2$$

= Estrogenic effect

The state of the s

Inventor: Sirbasku

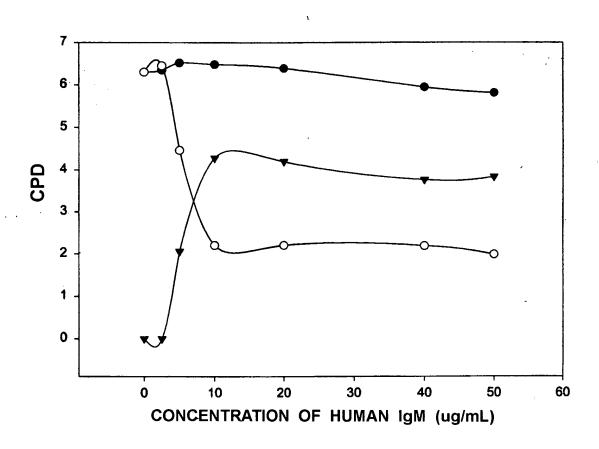
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 96 of 133

FIGURE 96

EFFECT OF HUMAN IgM ON MCF-7K CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

drup are deris

the word than and the

17

ļ:: []

ļ-i

= Estrogenic effect



Express Mail EL818623436US Inventor: Sirbasku

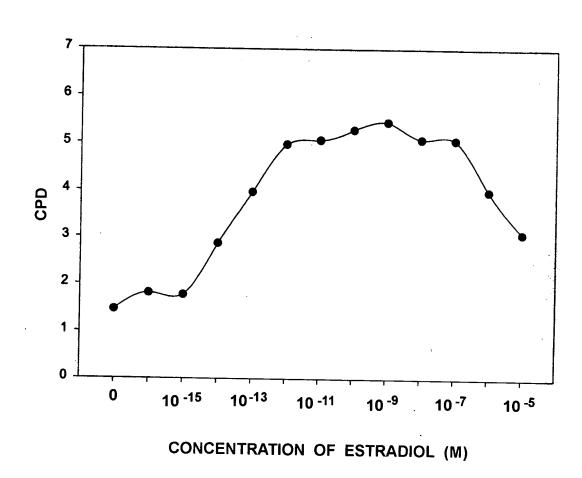
Atty Dkt. No. 1944-0080*0* Contact: C.G. Mintz (713) 238-8000

Page 97 of 133



FIGURE 97

EFFECT OF ESTRADIOL ON MCF-7K CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL HUMAN IgM



the first that the man tank is a few and the same and the

å.i

Express Widin ---Inventor: Sırbasku

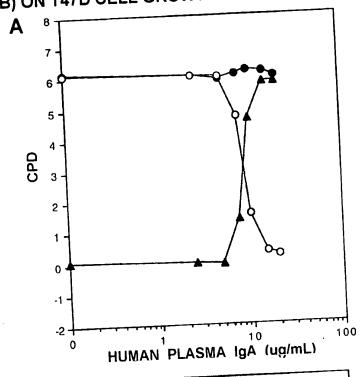
Atty Dkt. No. 1944-00800

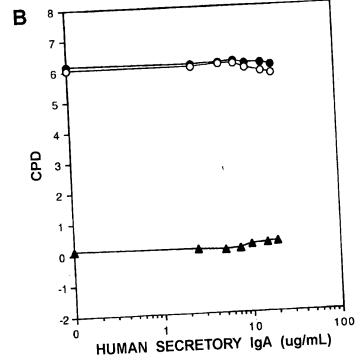
Contact: C.G. Mintz (713) 238-8000

Page 98 of 133

FIGURE 98

EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IgA (B) ON T47D CELL GROWTH IN SERUM-FREE MEDIUM





Closed circles = $+ E_2$ LEGEND: Open circles = $-E_2$

Closed triangles = Estrogenic ffect

[]! ŧ[] Į() the met the Hall and [] 179 ļ. The state of the s

trans after their

Inventor: Sirbasku
Atty Dkt. No. 1944-0080 7

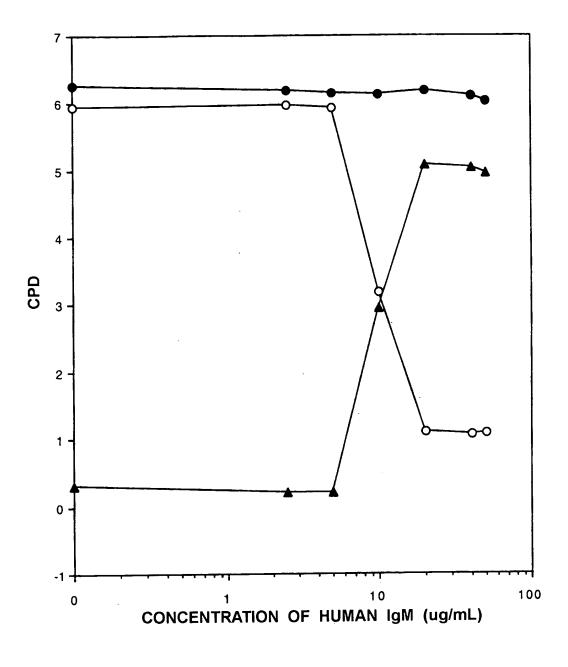
Contact: C.G. Mintz (713) 238-8000

Page 99 of 133

FIGURE 99

EFFECT OF HUMAN IgM ON T47D CELL

GROWTH IN SERUM-FREE MEDIUM



LEGEND: Closed circles = $+ E_2$

Open circles = $-E_2$

The life of the control of the contr

alle that that alle

Express Mail EL818623436US Inventor: Sirbasku

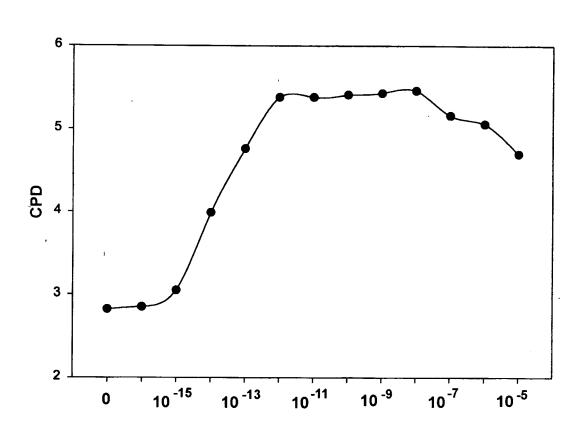
Atty Dkt. No. 1944-0080 0

Contact: C.G. Mintz (713) 238-8000

Page 100 of 133

FIGURE 100

EFFECT OF ESTRADIOL ON T47D CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL HUMAN IgM



CONCENTRATION OF ESTRADIOL (M)

11

had mad Bun mak I

Hard Breed

Express Mail EL61802545005

Inventor: Sıroasku

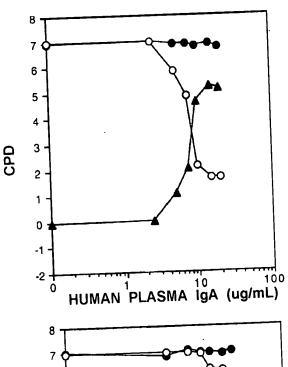
Atty Dkt. No. 1944-00800

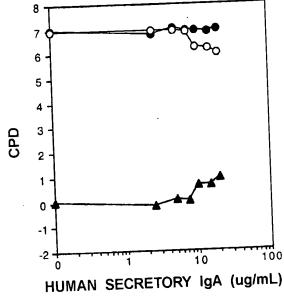
Contact: C.G. Mintz (713) 238-8000

Page 101 of 133

FIGURE 101

EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IgA (B) ON ZR-75-1 CELL GROWTH IN SERUM-FREE MEDIUM





Closed circles = $+ E_2$ LEGEND: Open circles = $-E_2$ Closed triangles = Estrogenic effect

Inventor: Sirbasku

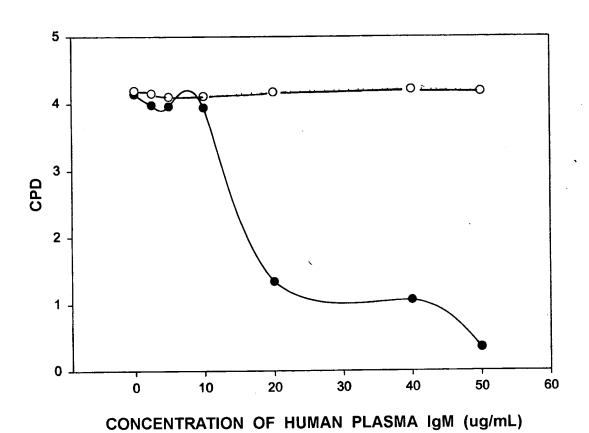
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 102 of 133

FIGURE 102

EFFECT OF HUMAN PLASMA IgM ON ZR-75-1 CELL GROWTH IN SERUM-FREE MEDIUM



LEGEND:

Par in day

171

1-1

. Ruft that after

Express Mail EL818023430US

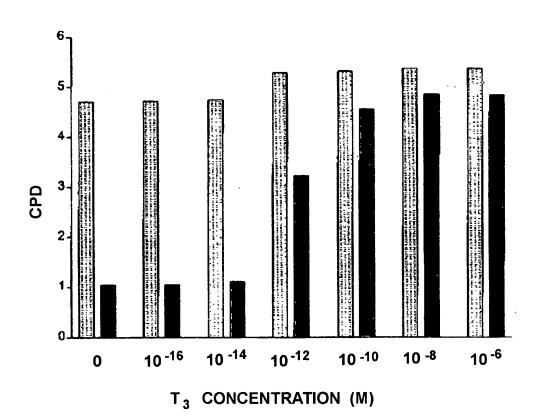
Inventor: Sirbasku

Atty Dkt. No. 1944-0080**0** Contact: C.G. Mintz (713) 238-8000

Page 103 of 133

FIGURE 103

EFFECT OF HUMAN IgM ON HT-29 CELL GROWTH IN THE PRESENCE OF INCREASING CONCENTRATIONS OF $\rm T_3$



LEGEND:

= T₃ Titration

 $= T_3$ Titration + 40 ug/mL lgM

[]

M

ļ.,

[]

Express Mail EL818623436US

Inventor: Sirbasku

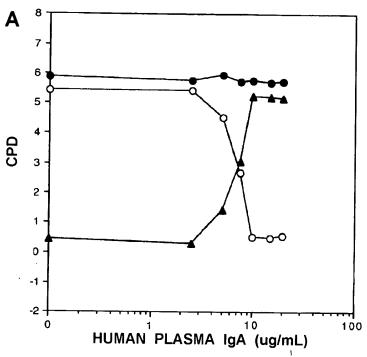
Atty Dkt. No. 1944-00800

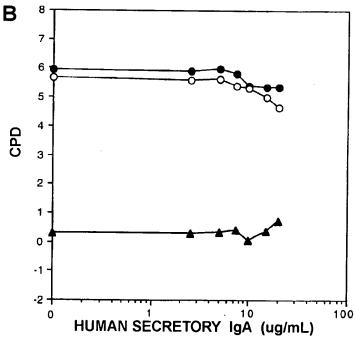
Contact: C.G. Mintz (713) 238-8000

Page 104 of 133

FIGURE 104

EFFECT OF HUMAN PLASMA IGA (A) AND SECRETORY IGA (B) ON LNCaP CELL GROWTH IN SERUM-FREE MEDIUM





LEGEND: Closed circl s = + E₂
Open circles = - E₂
Closed triangles = Estrogenic effect

Express Mail EL818623436US Inventor: Sirbasku Atty Dkt. No. 1944-0080**0**

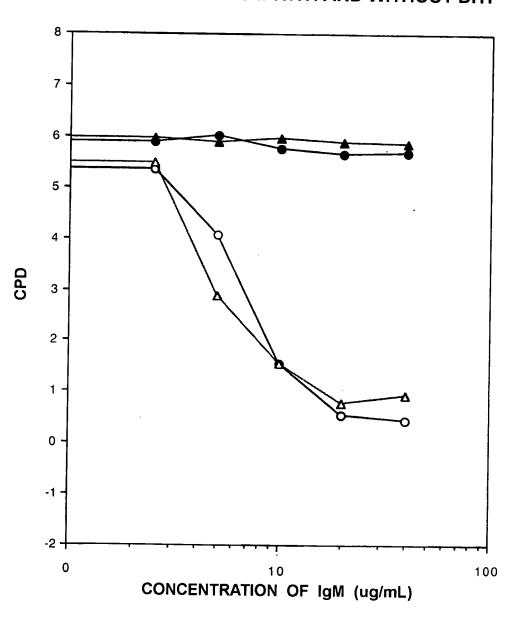
Contact: C.G. Mintz (713) 238-8000

Page 105 of 133

gc 105 01 155

FIGURE 105

EFFECTS OF HUMAN PLASMA IGM VS IGM DERIVED FROM MYELOMA CELLS ON LNCaP CELL GROWTH IN SERUM-FREE MEDIUM WITH AND WITHOUT DHT



And the first term than the control of the first term the first term that the first term that the first term than the first term that the first te

1-4

ŗ,

Inventor: Sirbasku

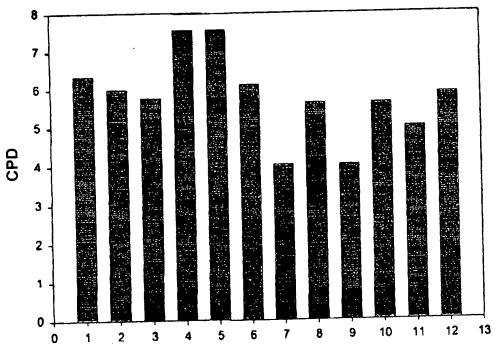
Atty Dkt. No. 1944-0080 7

Contact: C.G. Mintz (713) 238-8000

Page 106 of 133

FIGURE 106

ESTROGENIC EFFECT OF 50 ug/mL OF VARIOUS IgM'S ON SEVERAL DIFFERENT CELL LINES



CELL LINE AND TYPE OF IgM

LEGEND:

- 1. Human IgM on MTW9/PL2 Cells = 6.36 cpd
- 2. Mouse IgM on MTW9/PL2 Cells = 6.00 cpd
- 3. Rat IgM on MTW9/PL2 Cells = 5.77 cpd
- 4. Human IgM on H301 Cells = 7.57 cpd
- 5. Mouse IgM on H301 Cells = 7.56 cpd
- 6. Rat IgM on H301 Cells = 6.11 cpd
- 7. Human IgM on GH1 Cells = 4.12 cpd
- 8. Rat IgM on GH1 Cells = 5.83 cpd
- 9. Human IgM on GH3 Cells = 4.09 cpd
- 10. Human IgM on GH4 Cells = 5.41 cpd
- 11. Human IgM on MCF-7A Cells = 5.01 cpd
- 12. Human IgM on MCF-7K C IIs = 5.89 cpd

The second prints of the second state of the s

offer day days

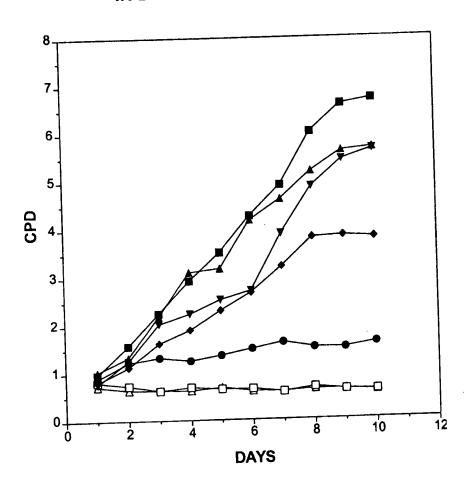
Inventor. Sirbasku
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 107 of 133

FIGURE 107

EFFECT OF TAMOXIFEN ON T47D CELL GROWTH IN DDM-2MF DEFINED MEDIUM



LEGEND: —— SFM + E₂

—— SFM - E₂

—— SFM + 10^{-9} M TAM

—— SFM + 10^{-8} M TAM

—— SFM + 10^{-7} M TAM

—— SFM + 10^{-6} M TAM

—— SFM + 10^{-6} M TAM

—— SFM + 10^{-5} M TAM

Inventor: Sirbasku

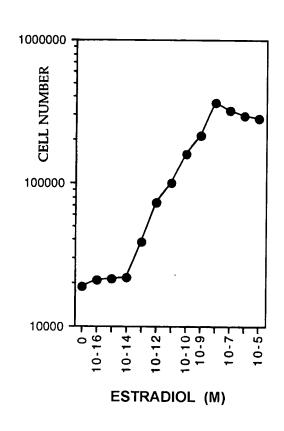
Atty Dkt. No. 1944-00800

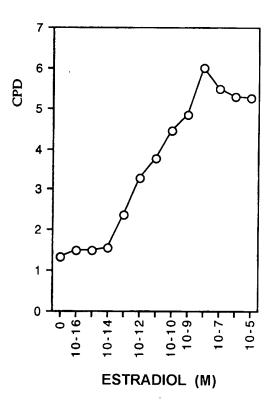
Contact: C.G. Mintz (713) 238-8000

Page 108 of 133

FIGURE 108

EFFECT OF INCREASING ESTRADIOL CONCENTRATIONS ON T47D CELL GROWTH IN SERUM-FREE AND PHENOL- RED FREE MEDIUM WITH 10⁻⁷ TAMOXIFEN





NOTE:

then must time.

#<u>F</u>=

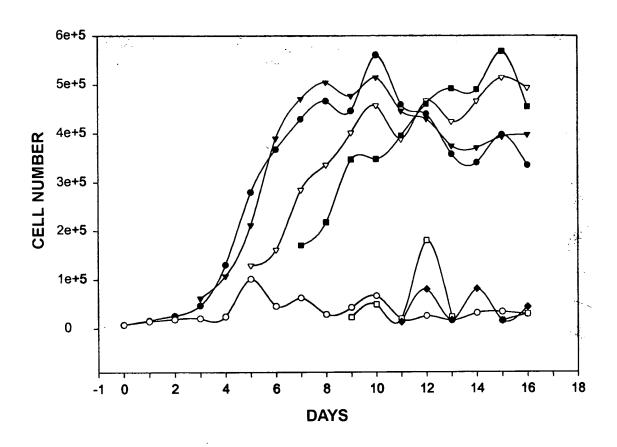
DATA ARE EXPRESSED AS BOTH CELL NUMBER AND CPD

Contact: C.G. Mintz (713) 238-8000

Page 109 of 133

FIGURE 109

E₂ RESCUE OF MTW9/PL2 CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL HORSE IgM



→ = E₂ Added on Day 0 LEGEND:

 $-\sim$ = No E₂

→ = E₂ Added on Day 2

 $- = E_2$ Added on Day 6

= E₂ Added on Day 8

= E₂ Added on Day 10

ļ.

Inventor: Sirbasku

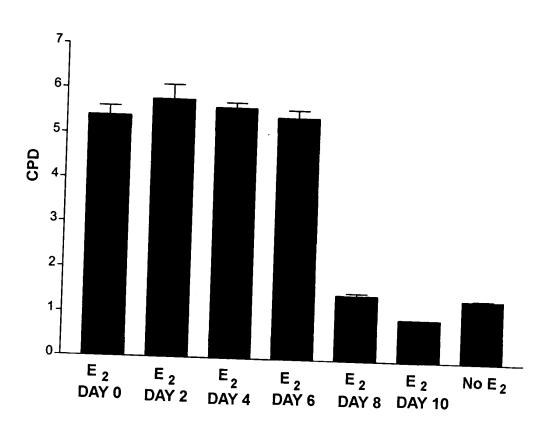
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 110 of 133

FIGURE 110

SUMMARY OF $\rm E_2$ RESCUE OF MTW9/PL2 CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL HORSE IgM



E 2 ADDITION (DAY)

first time the few man time time to be seen the seen time to be seen to be se

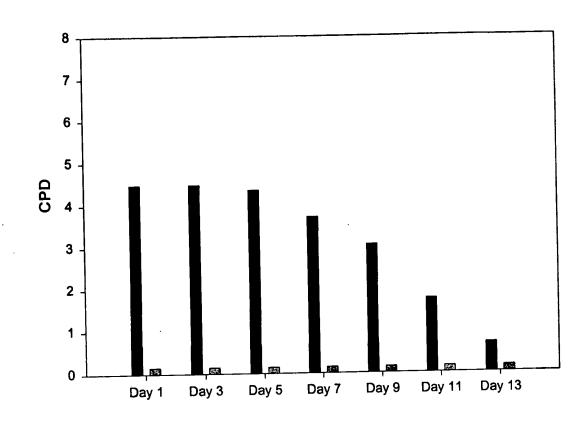
Inventor: Sirbasku Atty Dkt. No. 1944-0080**0**

Contact: C.G. Mintz (713) 238-8000

Page 111 of 133

FIGURE 111

E $_2$ RESCUE OF T47D CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL HORSE IgM



E₂ ADDITION (DAY)

LEGEND:

[] []

Ø

I

M

Home B in and

der the the day of the there there

$$= + E_2$$

Fyprece Mail EL818623436US

Inventor: Sirbasku

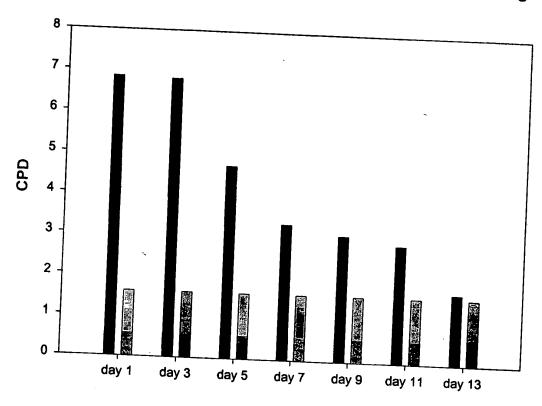
Atty Dkt. No. 1944-0080 **0**

Contact: C.G. Mintz (713) 238-8000

Page 112 of 133

FIGURE 112

ESTROGEN RESCUE OF MCF-7A CELL GROWTH IN SERUM-FREE MEDIUM WITH 40 ug/mL OF HUMAN SERUM IgM



E 2 ADDITION (DAY)

LEGEND:

The state of the s Bree may guest 0 H many Bath. of ≘ [] H ļ.

}=<u>+</u>

Ž=i

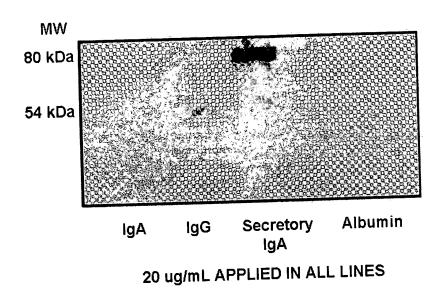
 Inventor. Sirbasku Atty Dkt. No. 1944-0080 **D**

Contact: C.G. Mintz (713) 238-8000

Page 113 of 133

FIGURE 113

DETECTION OF SECRETORY COMPONENT IN SECRETORY IGA WITH ANTI-SC ANTIBODY



IgA = Human Plasma

IgG = Human Plasma

Secretory IgA = IgA from Milk

Albumin = Human

Inventor: Sirbasku

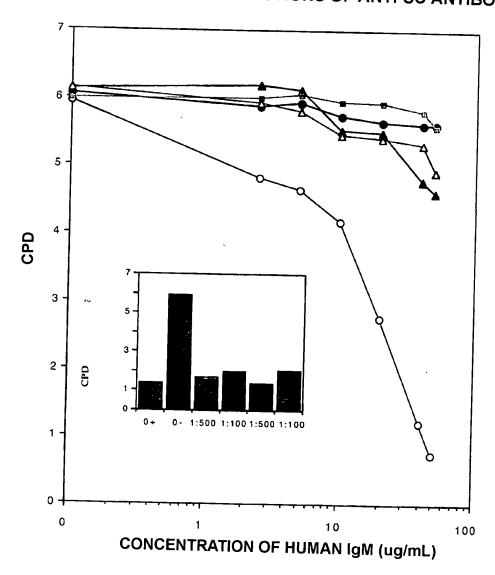
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 114 of 133

FIGURE 114

HUMAN IGM TITRATION ON T47D CELLS GROWN IN SERUM-FREE MEDIUM WITH DIFFERENT DILUTIONS OF ANTI-SC ANTIBODY



INSERT: EFFECT OF RABBIT SERUM ON T47D CELLS INCUBATED WITH 40 ug/mL HUMAN IgM

perty perty private many grows it is series in a constitution of the first many grows and the perty first than the

Money of the Hard Hands

Express Mail EL81862343608

Inventor: Sirbasku

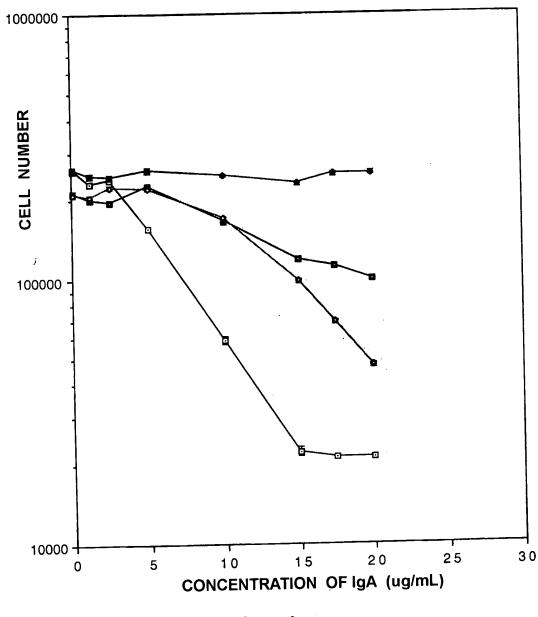
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 115 of 133

FIGURE 115

EFFECT OF IgA ON LNCaP GROWTH IN THE PRESENCE OF ANTI-SECRETORY COMPONENT ANTIBODY AT DIFFERENT DILUTIONS



LEGEND: — = Control

= 1:100 Dilution of Anti-SC Antibody
== 1:500 Dilution of Anti-SC Antibody
== 1:1000 Dilution of Anti-SC Antibody

Atty Dkt. No. 1944-00800

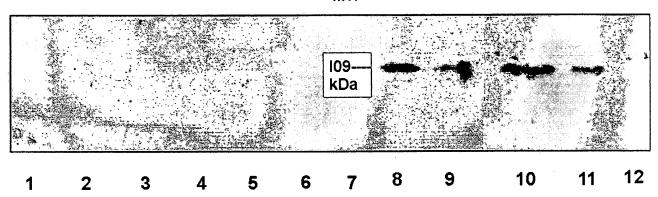
Contact: C.G. Mintz (713) 238-8000

Page 116 of 133

FIGURE 116

WESTERN BLOT: ANTI-SECRETORY COMPONENT





LEGEND:

- 1. MW
- 2. ALVA 41: 40 ug
- 3. ALVA 41: 20 ug
- 4. DU 145: 40 ug
- 5. DU 145: 20 ug
- 6. HUMAN FIBROBLAST: 40 ug
- 7. HUMAN FIBROBLAST: 20 ug
- 8. LNCaP: 40 ug
- 9. LNCaP: 20 ug
- 10. MDCK1: 20 ug
- 11. MDCK1: 10 ug
- 12. PC3: 40 ug

i-i

Express Mail EL818625456US Inventor: Sirbasku

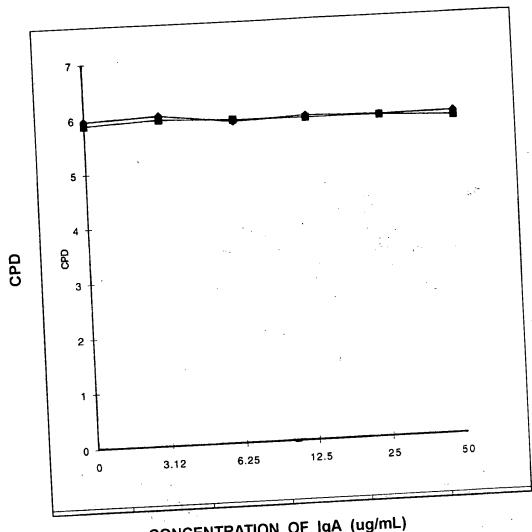
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 117 of 133

FIGURE 117

EFFECT OF HUMAN PLASMA IGA ON DU145 CELL GROWTH WITH AND WITHOUT DHT



CONCENTRATION OF IgA (ug/mL)

LEGEND:

then the test their many time it is seen that the test that the test that their time that the test the test that the test that the test the test that the test the test that the test the test

dest their officers of the first their states of the first the first their states of the first the first their states of the first the first their states of the first their states of the first the first the first their states of the first their states of the first the fir

[] []

Express Mail EL81862545000

Inventor: Sirbasku

Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

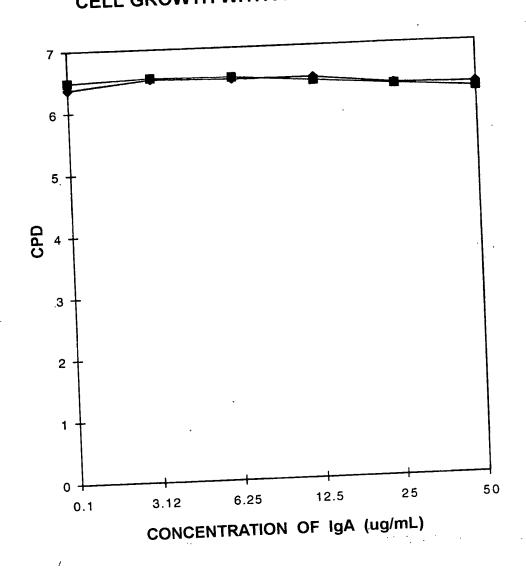
Page 118 of 133

[]

The first than and then the first term of the fi

Hard word ļ.

FIGURE 118 EFFECT OF HUMAN PLASMA IgA ON PC3 CELL GROWTH WITH AND WITHOUT DHT



LEGEND:

Inventor: Sirbasku

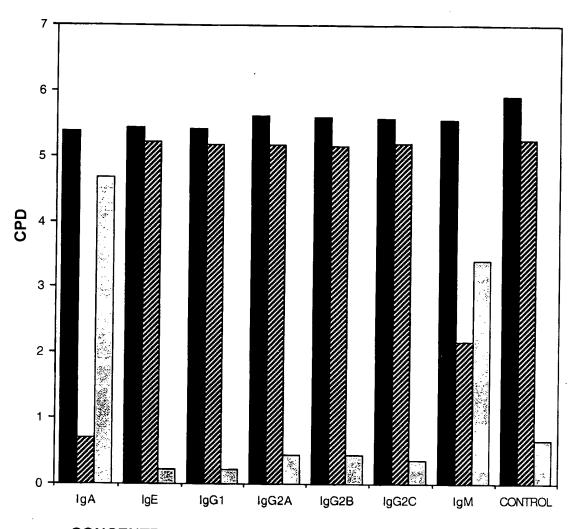
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 119 of 133

FIGURE 119

EFFECT OF RAT IMMUNOGLOBULINS ON MTW9/PL2 CELL GROWTH IN SERUM-FREE MEDIUM



CONCENTRATION OF RAT IMMUNOGLOBULINS (15 ug/mL)

LEGEND:

= Estrogenic effect

CONTROL IS SERUM-FREE MEDIUM ALONE ± E,

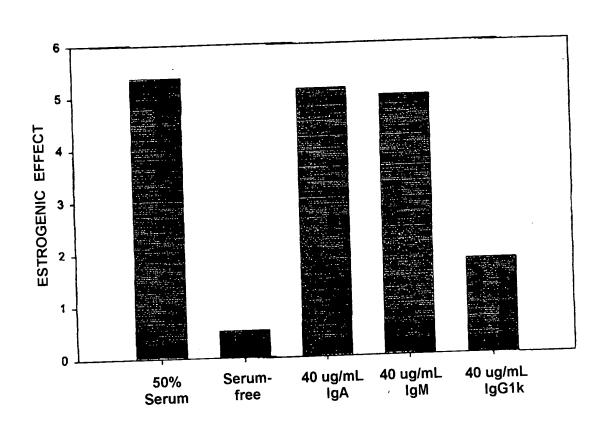
Inventor. Sirbasku
Atty Dkt. No. 1944-0080

Contact: C.G. Mintz (713) 238-8000

Page 120 of 133

FIGURE 120

ESTROGENIC EFFECT GENERATED BY IMMUNOGLOBULINS WITH T47D CELLS IN SERUM-FREE MEDIUM



IMMUNOGLOBULIN ADDED

The first that the other than the second the second that the s

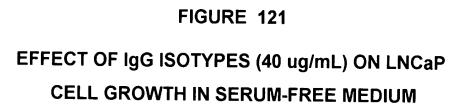
M

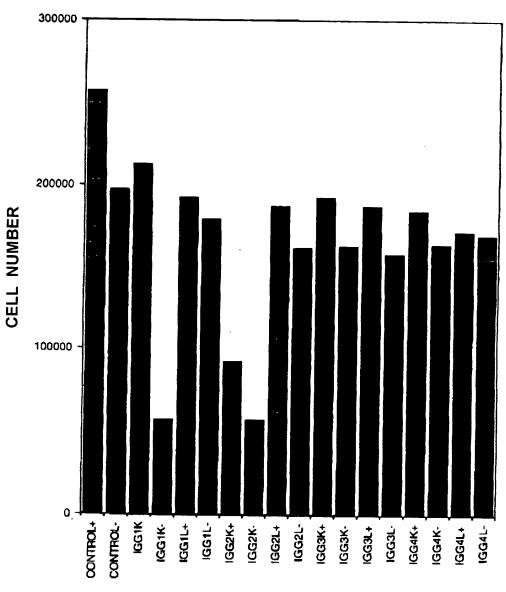
of the state of th

Inventor: Sirbasku

Atty Dkt. No. 1944-0080 Contact: C.G. Mintz (713) 238-8000

Page 121 of 133





IgG ISOTYPE ADDED

LEGEND:

= DHT Added

- = No DHT Added

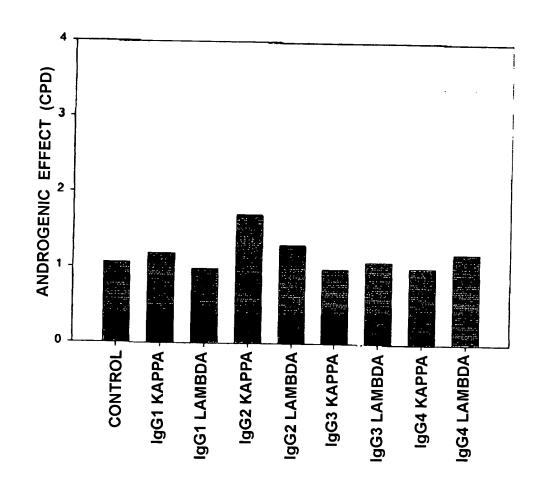
Express Mail EL818623436US Inventor: Sirbasku

Atty Dkt. No. 1944-0080 Contact: C.G. Mintz (713) 238-8000

Page 122 of 133

FIGURE 122

IgG ISOTYPE ASSAYS WITH LNCaP CELLS IN SERUM-FREE DEFINED MEDIUM ± DHT



The state of the s

Inventor: Sirbasku

Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 123 of 133

FIGURE 123

MODEL OF EARLY ONSET BREAST CANCER INCLUDING TGF-BETA

ER⁺ **BREAST CANCERS**

- (i) Inhibitory receptor(s) for IgA & IgM & IgG1
- (ii) Growth inhibition by IgA & IgM
- (iii) Little or no TGFB growth inhibition
- (iv) No TGFB receptors

NORMAL EPITHELIAL CELLS

įį. Ü 17 N

17 17 TH

dent dens de la Ress. Dente secuti

ļ.:

1. Inhibitory receptor(s) for IgA & IgM & IgG1 & TGFB

111

* * *

II. Growth inhibition by IgA & IgM & TGF β

ER-BREAST CANCERS

- (i) No functional receptors for IgA or IgM & IgG1
- (ii) No growth inhibition by IgA & IgM
- (iii) High sensitivity TGF β growth inhibition
- (iv) TGFB receptors present

Express Mail EL8180234 30000

Inventor: Sirbasku

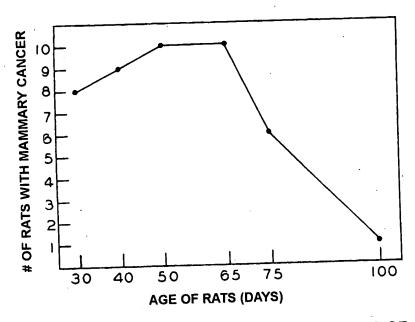
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

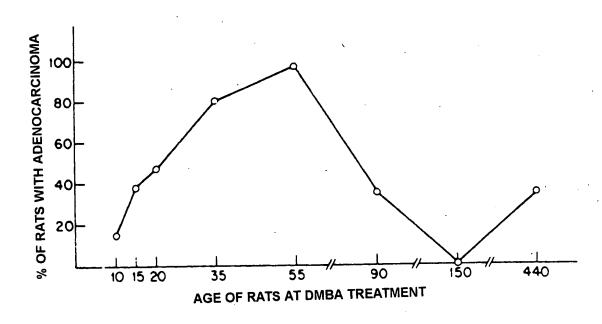
Page 124 of 133

FIGURE 124

EFFECT OF CARCINOGENS ON MAMMARY TUMOR INDUCTION IN RATS OF VARIOUS AGES



INCIDENCE OF MAMMARY CANCER IN GROUPS OF 10 FEMALE RATS OF VARIOUS AGES FED 3-MC, 100 MG



INCIDENCE OF MAMMARY ADENOCARCINOMA IN RATS GIVEN DMBA AT DIFFERENT AGES

Express Mail EL81802343003

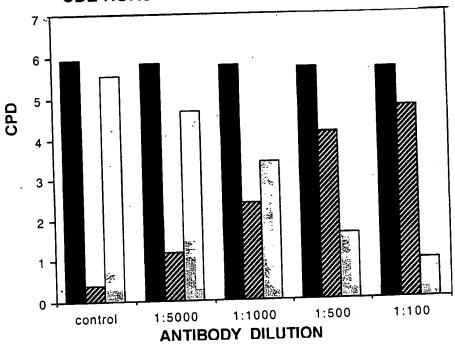
Inventor: Sırbasku

Atty Dkt. No. 1944-00800 Contact: C.G. Mintz (713) 238-8000

. Page 125 of 133

FIGURE 125

ANTI-HUMAN SHBG ANTIBODY IMMUNOPRECIPITATION OF THE ESTROGENIC ACTIVITY PRESENT IN CDE-HORSE SERUM WITH MTW9/PL2 CELLS

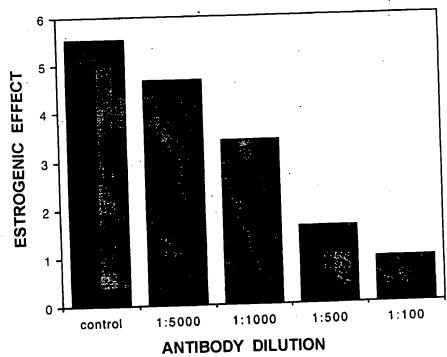


LEGEND:

= GROWTH IN 50% CDE WITH E $_{\mathrm{2}}$

= GROWTH IN 50% WITHOUT E 2

■ = E₂ EFFECT



Läpiess Mall EL818023436US

Inventor: Sirbasku

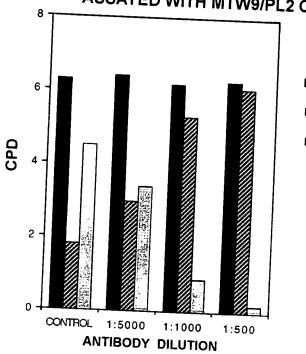
Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 126 of 133

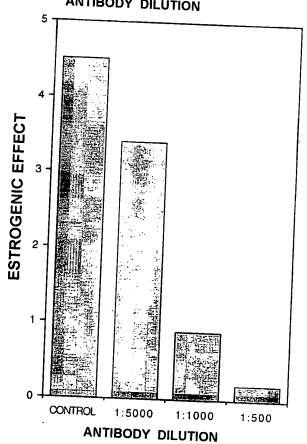
FIGURE 126

ANTI-HUMAN SHBG ANTIBODY IMMUNOPRECIPITATION OF THE ESTROGENIC ACTIVITY PRESENT IN CDE-RAT SERUM ASSAYED WITH MTW9/PL2 CELLS



= ESTROGENIC

EFFECT



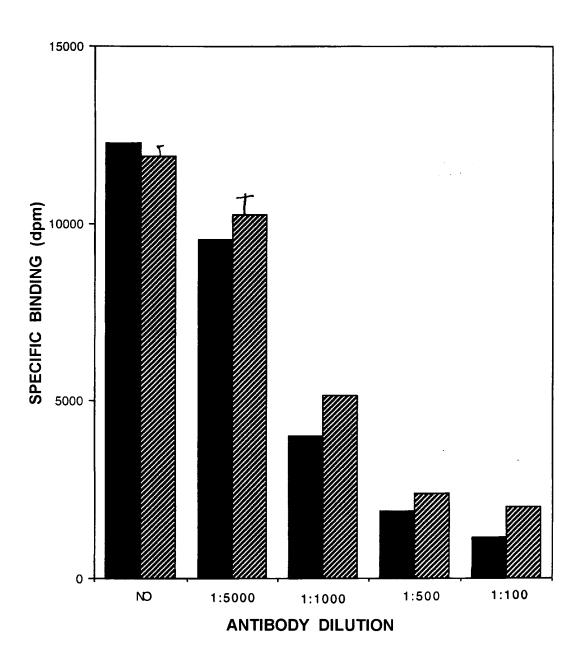
Express Mail El 818623436US Inventor: Sirbasku

Atty Dkt. No. 1944-0080**0** Contact: C.G. Mintz (713) 238-8000

Page 127 of 133

FIGURE 127

ANTI-HUMAN SHBG ANTIBODY IMMUNOPRECIPITATION OF THE LABELED STEROID HORMONE BINDING ACTIVITY PRESENT IN CDE-RAT SERUM



LEGEND:

■ = RAT

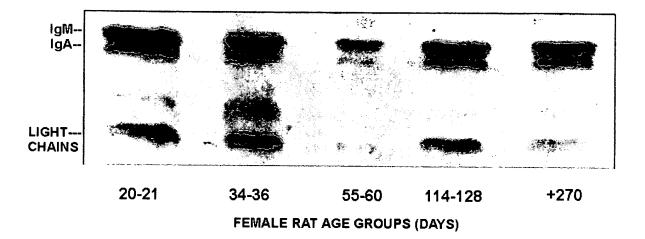
2 = HORSE

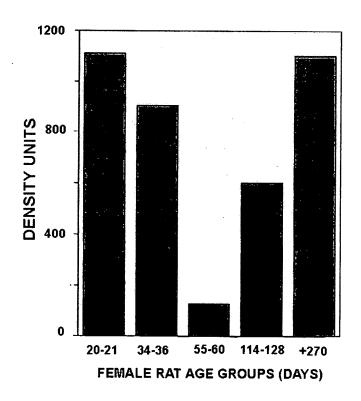


Inventor: Sirbasku
Atty Dkt. No. 1944-0080**0**Contact: C.G. Mintz (713) 238-8000
Page 128 of 133

FIGURE 128

WESTERN ANALYSIS AND DENSITOMETRY OF THE IMMUNOGLOBULIN LEVELS IN THE SERUM OF FEMALE RATS OF SPECIFIED AGE GROUPS





Inventor: Sirbasku

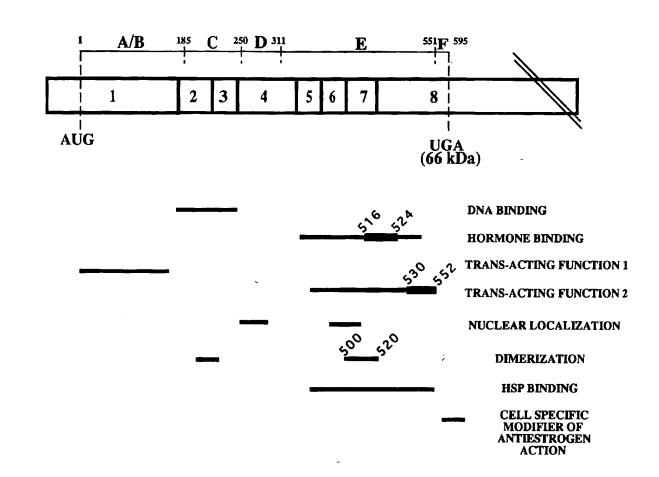
Atty Dkt. No. 1944-0080 9

Contact: C.G. Mintz (713) 238-8000

Page 129 of 133



STRUCTURAL AND FUNCTIONAL ORGANIZATION OF THE HUMAN ESTROGEN RECEPTOR-alpha



the first three times the second of the seco



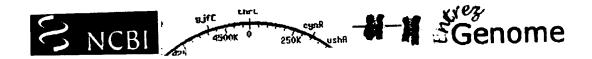
Inventor: Sirbasku

Atty Dkt. No. 1944-0080 1

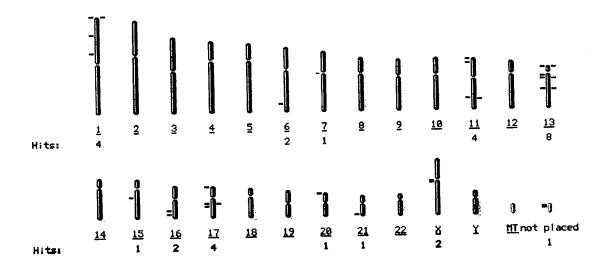
Contact: C.G. Mintz (713) 238-8000

Page 130 of 133

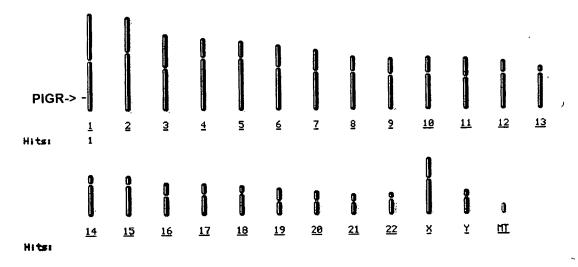
FIGURE 130



"BREAST CANCER" SEARCH - 31 "HITS"



"PIGR" (POLY-Ig RECEPTOR) SEARCH - 1 "HIT"



NOTE: THERE ARE NO BREAST CANCER "HITS" IN THE AREA OF THE POLY-IG RECEPTOR ON CHROMOSOME 1

Inventor: Sirbasku

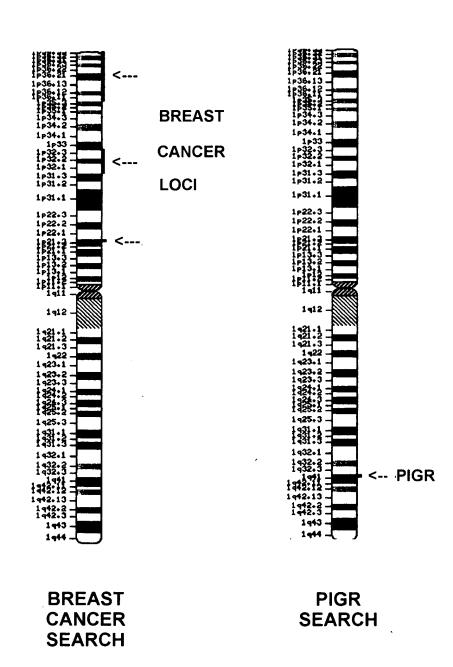
Atty Dkt. No. 1944-00800

Contact: C.G. Mintz (713) 238-8000

Page 131 of 133

FIGURE 131

CHROMOSOME 1





Inventor: Sirbasku

Atty Dkt. No. 1944-0080 D

Contact: C.G. Mintz (713) 238-8000

Page 132 of 133

FIGURE 132

CANCER AROUND THE WORLD, 1994-1997 DEATH RATES PER 100,000 (45 COUNTRIES)

Country		Colon & Rectum		L. 1		Prostate	
	M	ale	Fema	le	Fema	lei	Male
United	1	5.2	10	_	20		15.9
States†		27)	(2	3)	(14	4)	(20)
Australia‡	11	0.2			19.	_	19.0
	<u> </u>	10)	(1)	9)	(15	5)	(9)
Austria†		1.7	12	_	20.		16.9
		<u>(8)</u>	(14		(13)	(14)
Azerbaijan§		3.0	4.	2	8.	6	5.1
		11)	(43	= ;	(42		(41)
Bulgaria^	12	7.2 (0)	11.	711	15.		8.5
			(19		(31	_ =	(34)
Canada‡	10	6) 6)	10. (25	3	21.5		16.4
01:1	7	.0	6.	_	(10		(17)
Chile [^]		8)	(36		12. ⁻ (35		16.0
Chi		9	6.4	_ =	5.0	_	(19)
China¶^		6)	(37	VI.	(44)		-
Colombias		.8	5.1		9.1		12.6
Colombia [^]	(4		(40		(40)	3	(28)
Croatia#	22	5	11.5		18.5		13.0
Croatian	(5)L	(18)		(20)		(25)
Cubat	9.	4	11.3	-	14.9		20.8
	(34	_ا(را	(20)		(33)		(4)
Czech	34.		17.3		21.1	Ē	16.0
Republic§	(1		(3)		(12)	L	(18)
Denmark§	22.		15.6		27.6	Γ	19.9
	(5		(4)	_	<u>(1)</u>	L	(6)
Estonia§	18.	1]	12.2		18.5		12.8
	(16	==	(13)	_	(19)	<u> </u>	(27)
inland‡	12. (31	1	8.5		16.8		17.6
			(31)	<u>L</u>	(25)		(12)
rance‡	16.6		9.6 (29)		19.6		15.8
	20.8		14.0	_	(16)		(21)
Sermany†	(9)		(7)		21.7 (8)		16.6 (16)
	8.0	-	6.2		16.2		9.3
ereece§	(35)		(38)		(27)		(33)
Lings - AA	34.3		18.7		23.7		18.7
lungary^^	(2)		(2)		(6)		(11)
eland‡	22.5	Γ	13.3		26.1		18.8
Cialiu+	(7)	11	(9)		(2)		(10)
rael§	17.9		13.8		25.1		12.0
	(18)		(8)		(4)		(30)
				-		_	

FIGURES IN PARENTHESES ARE ORDER OF RANK WITHIN SITE AND SEX GROUP

SOURCE: MORTALITY DATABASE 1994-97 WORLD HEALTH ORGANIZATION, 1999

Country		Colon &						
Country		Rectum		السمسا	Prostate			
L	Male Female Female Male							
Japan**	17. (21	1 9) (2)		7.7 43)	5.1			
Kazakhstan	12.	6 8.		3.2	5.7			
) (30	- ; ;	34)	(39)			
Kyrgyzstan§	6.9 (39			0.6 37)	4.3 (43)			
Latvia‡	18.3	11.	8 1	7.3	11.5			
Lithuania§	18.2	11.	7 18	24) 3.7	(31) 15.2			
	(13			8)	(22)			
Macedonia§	10.8 (33)	"		3.1 (0)	6.2 (38)			
Mauritius§	6.0		8 8	0.0	7.7			
Mexico#	3.6			1) .3	(36) 12.8			
	(45)	(45	٠,,	9)	(26)			
Netherlands‡	. 17.7 (19)		:1	.0 3)	19.4			
New Zealand					(8) 19.8			
	_ (3)			7)	(7)			
Norway‡	20.0	14.7 (5)			23.2			
Poland§	16.4	11.0	16	1	<u>(2)</u> 11.1			
	(23) 18.1	(22)	1. 11.		(32)			
Portugal§	(15)	10.4 (24)			17.2 (13)			
Rep. of Moldova‡	16.2	11.1	18.	2	5.7			
Romania§	(25)	(21) 7.9	(21) 15.		(40)			
- Komania9	(32)	(33)	(32		8.3 (35)			
Russian Fed.‡	18.2 (14)	12.6 (12)	16. (28		7.2			
Slovakia‡	14.6	6.8	(20		(37) 12.2			
	(28) 23.9	(35)			(29)			
Slovenia§	(4)	14.0 (6)	21.2 (11		14.7 (23)			
Spain‡	16.4 (24)	10.0 (27)	17.5 (23)		13.9			
Sweden§	13.8	10.2	16.8	Г	(24) 21.4			
Trinidad &	7.8	(26) 8.3	(26) 21.5		(3)			
Tobago^	(37)	(32)	(9)		35.5 (1)			
Turkmenistan*	6.2 (40)	4.4 (42)	9.5 (38)	Г	1.4			
United Kingdom†	18.0	11.6	24.5	Γ	16.6			
	(17)	(17)	(5)		(15)			
Venezuela^	5.9 (43)	6.2 (39)	11.8 (36)		20.3 (5)			



Inventor: Sirbasku

Atty Dkt. No. 1944-0080

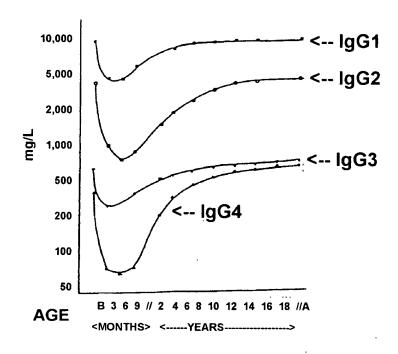
Contact: C.G. Mintz (713) 238-8000

Page 133 of 133



FIGURE 133

A: TYPICAL CONCENTRATIONS OF IgG SUBCLASSES DURING CHILDHOOD



B: IMMUNOGLOBULIN CHANGES WITH AGE

